REACTIVITY OF THE BICYCLO(3.3.1)NONANE SYSTEM

THESIS

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PART 1

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INTRODUCTION

One of the most interesting features of modern alicyclic chemistry is the increasing use of bridged bicyclic systems in developing physical-organic theory. Where the bridging of alicyclic rings results in conformational rigidity, the molecules can serve as models for testing reactions believed to have special steric requirements [1]. If, however, the molecule retains some flexibility, the semi-rigid framework provides aspects of conformation and molecular strain which are of potential interest.

An example of the latter category is the bicyclo(3,3,1) nonane system which can be formally derived from cyclooctane (1) by the incorporation of a methylene bridge between carbons 1 and 5, at the cost of some considerable degree of conformational mobility. Further methylene bridging between carbons 3 and 7 of bicyclo(3,3,1)nonane (2) forms the rigid tricyclic hydrocarbon adamantane (3) [2].

This formal derivation of 1, 2 and 3 has some chemical significance, e.g. Dale has shown that the three hydrocarbons form solid solutions in pairs, whereas none of them form a

solid solution with cyclodecane: this he reconciled with a similar globular shape (figure 1, A,B,C for 3,2 and 1) in contrast with non-globular cyclodecane (7) and therefore as evidence in favour of the saddle conformation (1) of cyclooctane.[3]

On the other hand, Allinger has calculated that deformation of an alternative centro-symmetric 'crown' conformation of cyclo-octane (4) can result in a 'stretched crown' (5) of lower energy content [4] and the latter conformation is generally assumed to be preferred [5,6], however, Dale has argued that the diamond-like 'saddle' conformation, with distorted bond angles to relieve the localised hydrogen crowding (1) is in better agreement with the available data [3,7]. Strain energy minimization calculations [8,9] (using a value of $\underline{109.5^{\circ}}$ for the C-C-C bond angles) suggest that several cyclo-octane conformations have comparable energies so that at ordinary temperatures a conformational mixture may be expected. However, infra-red and raman spectral evidence has been interpreted in favour of a single conformation [10] and calculations based on a bond angle of 116° [11] may afford results in accord with this.

Recently a hybrid conformation (6) called the 'boat-chair' by Hendrickson [8] has been established by X-ray analysis for the eight-membered ring in dimeric cyclo-octane peroxide [12]

and in cyclo-octane -1,2- trans dicarboxylic acid [11].
N.M.R. studies on deuterated (d_{14})-cyclooctanes have been interpreted by Anet as evidence for the boat-chair form and / or a twist boat-chair form being the major conformation(s) of cyclo-octane. His further studies of alkyl cyclo-octanes [14] have demonstrated the temperature dependant nature of the N.M.R. spectra and indicate that such compounds exist in a conformational equilibrium at ordinary temperatures, whereas Dale suggests that the low temperature N.M.R. data reported for perfluorocyclooctane [15] can only be accounted for in terms of a saddle conformation [16].

The presence of a bridging methylene group in bicyclo-(3,3,1) nonane limits the number of possible conformations to those represented in figure 2 (a-d), drawn from Dreiding models. Severe transannular crowding occurs in each conformer and these are summarised below.

Figure 2a. In the 'twin-chair' conformation one very serious interaction [17] between the endo-hydrogens on C_3 and C_7 is apparent. From models the H...H internuclear distance is only ca. 0.8 Å and the $C_3 \ldots C_7$ distance, 2.52 Å, and these must of necessity be relieved at the expense of the ideal chairs.

Figure 2b. A popular alternative mode of relief of the

3,7- methylene crowding is found in the 'boat-chair' form, and is associated with several individually smaller interactions: a 7,9- 'flagpole' interaction (H...H distance from models of 1.9 Å), a C_3,C_6 - and a C_3,C_8- endo-hydrogen ... pseudo-axial hydrogen interaction of some severity. An examination of models suggests that these interactions cannot simultaneously be mitigated by flexion of the boat ring, nor due to the constraint imposed by the chair ring can a twist-boat be realised, thus the eclipse of atoms attached to C_1,C_8 and C_5,C_6 cannot be relieved.

Figure 2c. Consideration of a 'twin-boat' conformer cannot be immediately excluded in such an inescapably crowded system, however the associated 'flagpole' interactions (C_3,C_9 and C_7,C_9) are accompanied by less severe hydrogen crowding (ca. 2.0 Å) below the plane of the rings involving the C_2,C_8- and C_4,C_6- endo-hydrogens. Again these interactions appear to be mutually reflexive this precluding simultaneous relief by ring flexion.

Figure 2d. The 'twin-boat' conformer is the only one which has any rotational freedom in the carbon framework and lateral distortion to relieve the flagpole interactions produces the 'twin-twist-boat' conformation with a severe transverse interaction of the C_2,C_6- endo-hydrogens, in addition to the interactions (somewhat lessened) present in the'twin-boat' conformation, as depicted.

Martin et al [18] have shown that a distorted (flexed) 'double-chair' conformation is adopted in crystalline 1-Bromo-p-sulphonyloxymethyl-5-methylbicyclo (3,3,1) nonan-9-ol (8), and infra-red data suggests that this is also the preferred conformation in solution. The C_3-C_7 distance was found to be 3.06 Å which results in an internuclear distance for the C_3,C_7-endo hydrogens of 1.8 Å (of the same order as hydrogen-hydrogen intra-annular distances calculated by Dunitz [19] for the medium rings). The relief of transannular crowding is achieved by distortion of the internal bond angles at C_2,C_3,C_4,and C_6,C_7,C_8 which have an average value of 114°, whereas the angles around C_1,C_5 and C_9 (average 110°) are very close to tetrahedral. The increase in peripheral bond angles has the effect of flattening the ideal chairs (figure 2a) at C_3 and C_7 such that the planes C_2,C_3,C_4 and C_6,C_7, C_8 are no longer parallel but are distorted outward through 17° and 16° respectively from the plane C_1,C_5,C_9. That no torsional distortion occurred was demonstrated by the equivalence of the $C_2 \ldots C_6$ and $C_4 \ldots C_8$ non-bonded distances, thus C_3, C_7 and C_9 are coplanar, as presumably are the hydrogens attached thereto.

The X-ray analysis of 3 - azabicyclo (3,3,1) nonane hydrobromide (9) has also been reported [20] and the results are in excellent agreement with those obtained for the carbocyclic system above: N...C_7 distance, 3.10 Å-, calculated C_7

endo H...H-N distance, 1,8 Å; with increases only in the peripheral angles.

The steric crowding of intra-annular hydrogen atoms present in 8-11 membered rings is associated with a special feature of medium-ring chemistry; The occurence of trans-annular hydride shifts in the course of reactions, involving cationic intermediates. The possibility of such behaviour exists for the bridged 8-membered of bicyclo(3,3,1)nonane and its derivatives, and some reactions have been reported in which the products can be explained by a specific C_3-C_7 hydride shift.

Ayer and Piers [21] treated the unsaturated alcohol 10, with sulphuric acid and obtained the ketone, lycopodine (13) by way of the cationic intermediates 11 and 12. The product 16, obtained from similar treatment of the epimeric alcohol 14, illustrates dramatically the stereospecificity associated with transannular reactions and supports the involvement of the intermediates outlined (11 and 15).

Weisner [22] reacted an unsaturated enol-ether, 17, under the same conditions and effected ring closure to a bicyclo (3,3,1)nonane derivative 21, of rearranged structure. Hydrolysis of the enol ether 17 to the trans-fused ketone 18 and subsequent ring closure to 19 might be expected to be promoted by the reaction medium but the transfer of hydride ion (19-20) is necessary to account for the final tri-substituted nature of the double bonds in 21.

These reactions indicate that a C_3-C_7 hydride shift may occur under suitable conditions although in each case there is a pronounced increase in the stability of the ions resulting from such a transfer. A rearrangement analogous to that proposed in 19 and 20 has recently been examined by Appleton and Graham [23] who subjected both ^{2}-7-exo-methylbicyclo (3,3,1) nonene (22) and 7-exo-methylenebicyclo (3,3,1) nonane (26) to formic acid and obtained in each case the same mixture of ^{2}-3-methylbicyclo (3,3,1) nonene, 93% (25) and 7-exo-methyl ^{2}-ene, 7%, (22). Thus an equilibrium seems to have been attained between the cationic species 23 and 24, favouring the latter. The possibility of such a shift occurring under non-equilibrating conditions in a symmetrical intermediate remained to be demonstrated. Therefore the behaviour of an unsubstituted model with respect to the efficacy of hydride transfer was of interest in the light of the X-ray crystallographic findings in these laboratories [18], and hence, a study of the solvolytic behaviour of suitable derivatives of 3-exo and 3-endo-bicyclo (3,3,1) nonanols was undertaken.

DISCUSSION

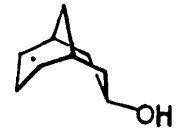
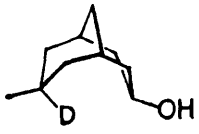
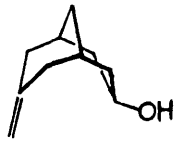
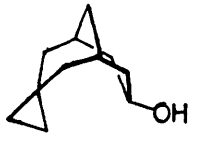
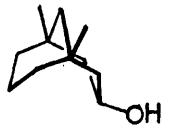
Since we chose to investigate the effects of transannular crowding inherent in the bicyclo(3,3,1)noname system by examining the solvolytic behaviour of suitable derivatives of t 3-exo and 3-endo alcohols, the ground state conformational properties of these compounds are relevant.

The assignment of configuration to the epimeric alcohols (30 and 39) is based upon the methods of preparation: the exo-epimer is obtained in high stereospecificity (accompanied by 2-exo alcohol) by hydroboration of ^{2}-bicyclo(3,3,1)nonene or by alkali-metal reduction, in moist ether (or liquid ammonia) of bicyclo(3,3,1)nonan-3-one and is consistent with a preferential attack on the exo face of the substrate molecules (27 and 28), as is the formation of the endo alcohol by hydride reduction of the parent ketone. Similar results have been associated with the reduction of 1,5 dimethylbicyclo(3,3,1) nonan-3-one [24], -pelletierine (29) [25] and 7-exo-methylbicyclo (3,3,1)nonan-3-one [26].

Conformational analysis suggests that the introduction of an exo-substituent at the 3 or 7 positions would not alter the basic 'flexed' double chair conformation associated with bicyclo(3,3,1)nonane (figure 1B), but rather would destabilise the other possible conformations of the substituted ring to a considerable extent. Evidence supporting this is to be found in the NMR data for the simple 3-exo alcohol (30)

TABLE 1.

NMR : Carbinyl Proton Signal (CCl_4 solution).

	COMPOUND	CHEMICAL SHIFT τ	J_{aa} c/s.	J_{ae} c/s.	DISTORTION	M.
30		5.68	11.0	6.0	ca 19°	9
31		5.80	11.0	6.0	ca 19°	9
32		5.80	11.0	6.0	ca 19°	9
33		5.63	11.0	5.5	ca 21°	7
34		5.20	11.0	6.0	ca19°	9
35		5.62[36]	11.4	6.6	ca 25°	9

M : Multiplicity

and related compounds (table 1).

The NMR spectra of 30, 33 and 35 are reproduced in part in Figure 3. The signal for the C_3 hydrogen atom can be treated as the X part of an A_2B_2X system since there is little possibility of significant coupling with protons on carbon atoms further removed than C_2 andC_4 [27]. The apparent coupling constants derived from a first-order analysis of the symmetrical 7 or 9 line signals for the carbinyl protons (table 1) can be seen to be in only approximate agreement with those expected for an ideal double chair (Figure 4A) on the basis of the modified Karplus expression derived by Williamson and Johnson [28]. Whilst it has been shown that the coupling constant is not solely dependent on the dihedral angle but also on the system under consideration [29], it seemed prudent to consider the effect of the increase in the peripheral CCC bond angles on the dihedral angles of the A_2B_2X system involved. The first effect to be considered in enlarging the CCC bond angle from tetrahedral to approximately 114-116° must surely be associated with a decrease in the HCH bond angles from the tetrahedral value at C_2 and C_4 (and perhaps associated changes in the HCC angles), thus the projected dihedral angle, AB, for protons A and B would be less than 120°. The second effect, a flattening of the rings, has been observed [18] and results in a smaller projected dihedral angle for C_1C_4 (Figure 4B) The observed

coupling constants can be seen to evidence both of these effects (Figure 4C) for the projected dihedral angles, AX and BX, associated with coupling constants J_{AX} = 11.0 and J_{BX} = 6.0 c/s infer AB = 112° or an HCH angle at C_2 and C_4 of the order of 102°, and a C_1C_4 dihedral angle of ca 41° (making allowance for non-tetrahedral geometry at C_3 also). This estimate of the deviation from ideality (60°) implies that the plane $C_2C_3C_4$ is distorted outwards by an angle of 19° from the ideal chair conformation and hence makes an angle of 139° (rather than 120°) with the plane $C_1C_2C_4C_5$. This estimate is in agreement with the distortions observed in 8 by X-ray crystallography : the plane $C_2C_3C_4$ is distorted outward from the plane $C_1C_5C_9$ by 17° and since the arrangement of atoms around C_1 and C_5 is close to tetrahedral [24], the planes $C_1C_2C_4C_5$ and $C_2C_3C_4$ make an angle of intercept of the order of 137° (and the corresponding planes $C_1C_8C_6C_5$ and $C_6C_7C_8$ an angle of 136°). The NMR data thus indicates that the cyclohexanol rings in compounds 30 - 35 are in chair conformations (flexed outward at C_2 and C_4) but the estimates of the distortion present in the 6 - membered ring need not be relative, in view of their dependence upon dihedral angles evaluated from coupling constants.

The NMR evidence which supports a double chair conformation for each of the compounds 30 - 35 is the values of the chemical shift of the C_3 proton (H_x, table 1) which are all lower than

the usual range of 6.0 - 6.7 for axial carbinyl protons of cyclohexanol derivatives [30]. The low values associated with 33 and 34 are perhaps not unexpected considering the nature of the substituent group at C_7, and serve to indicate clearly the preferred conformation. The values associated with 30 and 35 are interpreted as resulting from transannular deshielding associated specifically with the proximity of the C_3 and C_7 endo hydrogen atoms (presumably resulting in mutual deshielding although the signal for the C_7 - endo hydrogen cannot be distinguished from the methylene envelopes), and is intrinsically associated with the double chair conformations. That a similar effect is observed in 31 and 32 which are assuredly in double chair conformations is taken as confirmatory evidence. Thus the NMR data is consistent with the view that the introduction of an exo 3 or 7 substituent does not markedly affect the preferred 'flexed' double chair conformation. The specificity of the transannular deshielding by proximal hydrogen atoms in the 3 - exo - bicyclo (3,3,1) nonanols 30, 31 and 35 is supported by the observed value for the carbinyl proton of 3 - exo - bicyclo (3,2,1) octanol (48, 6.25) [31] in keeping with the different spatial arrangements of atoms, and by the value of the carbinyl signal of 36, a derivative of 7. azabicyclo (3,3,1) nonan - 3 - exo - ol (5.45) [32].

The NMR spectra of 3 - exo - bicyclo (3,3,1) nonanol, of

the 3 - exo acetate and of the 3 - exo toluene - p - sulphonate show identical 9 line signals for the C_3 protons (J_{AX} = 11.0 J_{BX} = 6.0 c/s) at 5.68, 4,62 and 4.92 respectively, and indicate the preference of a flexed double chair conformation in all three compounds.

To date there is only one example of a 3 - exo - bicyclo (3,3,1) nonane existing in part in a conformation other than a double chair, the 9 - aza analogue 3 - granatanol (37). Infra-red studies in CS_2 indicate the presence of some intramolecular hydrogen bonding attributed to the chair-boat conformer 38, present to the extent of about 10% [33].

The introduction of an endo - hydroxyl group at the 3 position, however, increases the extent of transannular crowding in the molecule. Conformational analysis of this system is complicated somewhat by the over - emphasis of a tetrahedral disposition inherent in atomic models. It seems probable that the peripheral CCC bond angles are of the order of 114 - 115° and approximate diagrams of space - filling models, incorporating such bond angles are shown in profile in Figure 5. As a result the 'flexed' chair - boat conformation, A, corresponding to 39, has important deviations from ideality : the chair cyclohexane ring is distorted outward at C_7 by 17° and the boat ring is flattened at C_3 by a similar distortion. The 'flagpole' interaction and the $C_2C_4C_7$ - endo hydrogen crowding are simultaneously aleviated and the associated

eclipsing of the C_1 - C_2 and C_4 - C_5 hydrogen atoms is modified slightly. The geometry of the system still does not appear to accomodate significant 'twist'-form in the boat ring, consequently the boat ring may be undistorted other than by the changes in peripheral angles.

The 'flexed' double chair conformation, B (40), still retains a considerable transannular interaction between the C_7 - endo hydrogen and the endo hydroxyl group (compare figure 1B which represents a H...H distance of 1.8 Å for the C_3,C_7 - endo hydrogens). This specific interaction could be alleviated by further angle distortion associated with a marked increase in strain and increasing crowding of the 1,3 related, equatorially disposed hydrogen atoms on C_2,C_8 and C_4,C_6.

The boat-chair conformation, C (41) is destabilised relative to A by the increase in strain associated with two endo hydrogens (C_6C_8) interacting with a hydroxyl group rather than a hydrogen atom.

The relative stability of B and C is more difficult to assess, but doubtless the dominating factor will be the manner in which the endo hydrogen...hydroxyl interactions are accomodated in each molecule. If this is achieved by further flexion of the carbocyclic rings they will each approach the eclipsed 'transition' conformation and it is difficult to say on which side the equilibrium will lie.

The absence of such transannular endo hydrogen hydroxyl

interactions in A would thus suggest this as the preferred conformation though little is known of the strain associated with a locked boat ring, and an equilibrium between all three conformations may exist. The fourth possibility, a double-boat conformation and associated twist-boat conformations are discounted due to extensive multiple hydrogen crowding on the endo face of the molecule.

Recent results in the homologous ring system tricyclo $(5.3.1.1^{2,6})$ dodecane (50) may enable a distinction between B and C to be made. A derivative of this ring system, 51 (X = p-iodobenzoate) was found to exist, in the solid state, in a conformation with significant deviations from ideal chairs [34] (compare 50). With reference to plane $C_1C_{11}C_7$, $C_2C_{12}C_6$ is flexed 8° outward from C_9, $C_8C_9C_{10}$ 40° outward from C_{12} and $C_3C_4C_5$ 41° outward from C_{11}, in this manner the molecule accomodates the C_4 - C_{11} endo hydrogen interaction and the severe C_9 endo hydrogen...C_{12} endo hydroxyl group interaction without torsional distortion. This indicates that the degree of distortion necessary to accomodate a chair cyclohexanol ring (figure 5, B and C) is associated with less overall strain in a distorted double chair (B) than in the boat chair conformation (C). In 51, the cyclohexanol ring is constrained in a chair conformation by two fused cyclohexane rings and the finding of a double chair conformation cannot be applied per se to the simple 3 - endo

alcohol (40) in which the cyclohexanol ring is free to adopt an alternative conformation (39) which places the hydroxyl group in a equatorial position.

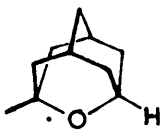
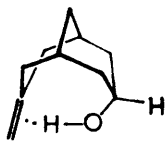
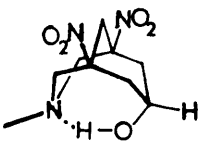
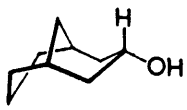
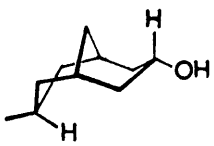
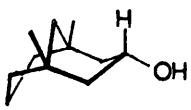
Nuclear Magnetic Resonance spectroscopy is today one of the best methods available for the conformational analysis of cyclohexane derivatives [27]. The analysis of the bicyclo (3,3,1) nonane system is to some extent simplified by the fact that the inherent geometry precludes the inversion of one chair cyclohexyl ring with an axial substituent into another chair ring with the substituent equatorial. In this respect the bicyclic molecules are ideal 'fixed' models for the study of cyclohexane boat-chair equilibrium.

The marked stability of the 'fixed' double chair conformation (30) of the 3 exo alcohol, relative to alternative conformations, was demonstrated by variable temperature studies. The 9 - line signal observed for the carbinyl proton was unchanged over the range -50° to $117^{\circ}C$. This suggests that the energy barrier to chair-boat inversion may be considerable (compared with that of simple cyclohexane rings) and this in turn may be a reflection of the number of unfavourable interactions present in the transition to boat forms, since twist-boat forms cannot be accomodated individually.

Both 60 and 100 Mc. NMR spectra of the 3-endo alcohol (39) are shown in part in Figure 6. The signal for the carbinyl proton in each case is asymmetric and more complex than a first-

TABLE 2

NMR DATA : Carbinyl Proton Signal (CCl_4 solution).

	COMPOUND	CHEMICAL SHIFT τ	$J_{AX} + J_{BX}$	M	REF.
45		6.10	6	m	-
46		6.37	9*	7	-
47		5.80	9*	m	32
40		6.22	18	a	-
42 41		6.20	ca 17	a	-
43. 42		6.15	15.6	9	36

M : Multiplicity m : symmetrical multiplet
a : asymmetrical multiplet

* In the presence of D_2O, see Section II

order A_2B_2X system. As a reasonable approximation a signal shows a first-order splitting when the chemical shift between it and the nuclei with which it is coupled is ten times larger than the coupling constants which cause the splitting [27]. This ratio in both the 60 and 100 Mc spectra is less than ten and a second order (or higher) signal is obtained. There is however one property which is common to both first order signals and those of higher order. The width of the signal between the extreme outside lines is independant of order and corresponds to the sum of the coupling constants involved [27].

When the derived value of $(J_{AX} + J_{BX}) = 18.0$ c/s, is compared with the sum of the coupling constants associated with the various conformations in Figure 7, it is clear that the cyclohexanol ring is in a boat conformation, in spite of the difficulties associated with obtaining the individual coupling constants. Several examples of 3-<u>endo</u> substituted bicyclic compounds are shown in Table 2 and these can be seen to fall into two distinct classes when the values of the sum of$(J_{AX} + J_{BX})$ are compared with Figure 7. Compounds 46 and 47 are known to exist in double chair conformations (see section II) and with 45, a bridged double chair, clearly correspond to conformation type B (figure 7) whereas 40, 42 and 43 are in accord with type D.

There are two factors which can invalidate this traight-forward treatment, the first is the occurence of long-range coupling in which the carbinyl proton may couple with protons

on carbons other than those on C_2 and C_4, and the second is that the complex signal may be a time average, arising from a rapid conformational equilibrium.

The occurence of long-range coupling in cyclohexane systems has infrequently been observed involving 1,3 diequatorial protons (J_4) and is associated with a value of 1 - 2 c/s [27] although values as high as 7 c/s have been observed in some strained bicyclic systems [35]. J_4-coupling is more likely to occur in a double chair conformation (40) than in a chair-boat (39) due to the spatial arrangements of the hydrogens involved, and cannot be discounted in view of the inherent distortion associated with the system under investigation. The NMR data is consistent with a distorted double chair conformation (40) only if there is appreciable long-range coupling, of the order of 5 - 7 c/s (in which case $J_{AX} + J_{BX}$ 11 - 13 c/s since the sum of all the coupling constants involved is 18 c/s). The magnitude of the long-range coupling was determined from the 100 Mc NMR spectrum of the 2,2, 4,4 - tetradeutero - 3 - endo alcohol 72. The carbinyl signal at 6.13 (in CD_2Cl_2 - d_6 acetone) was a singlet of outside line separation, 8 c/s, corresponding to twice the sum of the coupling constants involved. Since $J_{HH} = 6.55\ J_{HD}$ [35] the sum of the expected deuterated A_2B_2 coupling with H_X is ca 2.7 c/s, hence the total long-range coupling involved is only of the order of 1.3 c/s which is of insufficient magnitude to affect the arguments favouring the chair-boat conformation (39).

Variable temperature studies (100 Mc) showed that the complex signal observed for the 3 - endo alcohol at 30° (Figure 6) was unchanged at 117° (in tetrachloroethylene) and low temperature studies showed little change but these were complicated by solubility problems, whereas the sharper signal of the tetradeutero alcohol 72 was more readily discerned with accuracy. Over the temperature range 45° to -65°C the singlet carbinyl signal, in the latter case, showed no change in chemical shift (6.13), nor in half-band width. This would seem to preclude the possibility of a conformational equilibrium since it is exceedingly unlikely that the carbinyl protons in 39, 40 and 41 all have the same chemical shift. Thus in the absence of evidence to support a plurality of equilibrating conformations for the 3 - endo alcohol, the agreement of the NMR data with that expected for a 'flexed' chair-boat, the preferred conformation by analysis, may be taken as definitive.

The results obtained from a first-order analysis of the carbinyl signal for the 1,5-dimethyl 3 - endo alcohol (43, Figure 6) have been reconciled with both a boat-chair conformation (43) [24] and an equilibrium of the two possible chair-boat conformations 43 and 44 [36]. If the observed values (J_{BX} = 9.0, J_{AX} = 6.6 c/s) refer to a single conformation, the associated dihedral angles infer a 'flexed' boat conformation for the cyclohexanol ring with the C_3 atom 'hinged'

outward at C_2 and C_4 by 25° which is a greater deviation than that which can be inferred for the simple 3 - endo alcohol (5 - 15°). This is meaningful when the 1,2 eclipsing interactions inherent in a boat conformation are considered, for the greater relief of two such methyl...hydrogen interactions in 43 compared with two hydrogen...hydrogen eclipsings in 39 is associated with greater deformation of the boat ring in the former case.

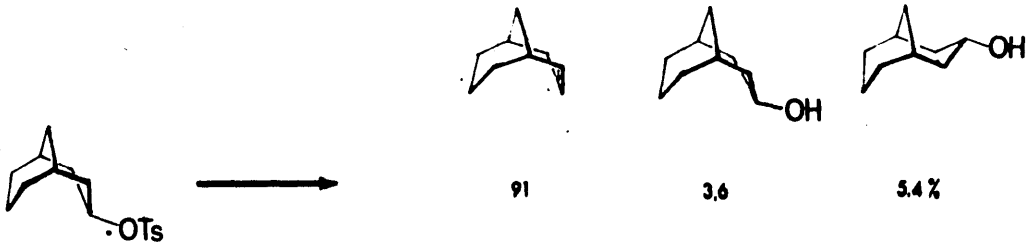
The 3 - endo tosylate, has never been obtained in a crystalline state, and was found to be a very unstable oil, consequently satisfactory NMR data has not been obtained, however, the available data (100 Mc) would suggest that the signal for the C_3 - proton occurs at 5.45 as a first order septuplet with apparent coupling constants J_{BX} = 14 c/s and J_{AX} = 7 c/s and a base line width of 42 c/s, which are not inconsistent with a 'flexed' chair-boat conformation corresponding to 39.

To aid in the clarification of the preferred conformation of 3 - endo bicyclo (3,3,1) nonanyl compounds, an X-ray crystallographic study of 1 - Bromo - 3 - endo bicyclo (3,3,1) nonanol is under investigation in this department.

TABLE 3.

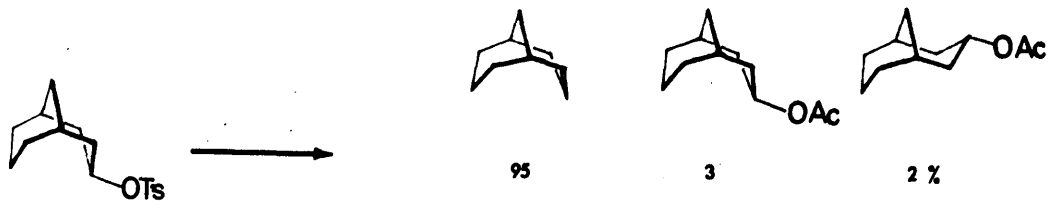
SOLVOLYSIS PRODUCTS

Aqueous Acetone , Li_2CO_3



	91	3.6	5.4 %
	72.8	19	8.2 %
	* 71	20.5	8.5 %

Acetic Acid , NaOAc



	95	3	2 %
	91	6.3	2.7 %
	* 90.6	6.6	2.8 %

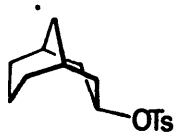
* Corrected for epimeric impurity.

The products of solvolysis of 3-exo and 3-endo-bicyclo-(3,3,1)nonanyl tosylates are shown in Table 3. The percentage of olefin produced in acetolysis is considerably higher than that produced from cyclooctyl brosylate (47%),[37] and is comparable with the product distribution of cyclodecyl tosylate (97%, cis and trans olefins).[38] Although the elimination product dominates the distribution from both 3-exo and endo tosylates in both solvent media, an increase can be seen in the ratio of substitution to elimination products in aqueous acetone and the net inversion of configuration of the substitution products are consistent with the greater nucleophilic character associated with this medium. The preferred formation of exo acetate in the acetolysis of both tosylates may reflect certain steric factors associated with the intermediate cation similar to those governing the reduction of the 3-ketone, although the degrees of stereospecificity are not comparable. Each of the solvolysis products was subjected to the solvolysis conditions and recovered without change.

The kinetics of the aqueous acetone solvolysis were not studied, but the rate data for the acetolysis reactions are shown in Table 4 (cf. Appendix A). The 3-exo tosylate (52) was obtained as a highly crystalline if somewhat unstable solid, and could be recrystallised at low temperatures (-10°C) whereas the endo tosylate (53) was always obtained as an oil,

TABLE 4.

ACETOLYSIS RATE DATA.

TOSYLATE	RATE CONSTANT (sec^{-1}.)	TEMPERATURE
	5.78×10^{-5}	25.0°C
	1.14×10^{-3}	50.0°C
	9.25×10^{-3}	70.0°C
	2.31×10^{-2}	80.0°C
52	$\Delta H^{\ddagger} = 23.0$ Kcal./ Mole.	
	$\Delta S^{\ddagger}_{25^{\circ}} = -0.8$ e.u.	
	*7.4×10^{-5}	25.0°C
53		
	$\Delta H^{\ddagger} = 22.4$ Kcal./ Mole.	
	$\Delta S^{\ddagger}_{25^{\circ}} = -1.8$ e.u.	
	9.25×10^{-5}	25.0°C
	1.86×10^{-3}	50.0°C
98		

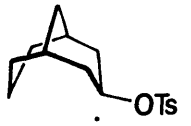
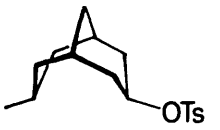
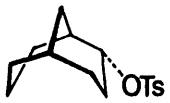
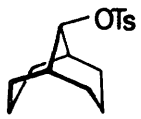
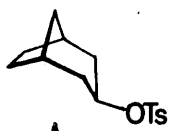
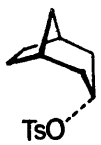
*Due to difficulty in purification, the rate data is only approximate.

containing approximately 6-9% of its epimer, but free from unreacted alcohol. The accuracy of the kinetic data of the two compounds are not of the same order, but, nevertheless the endo-tosylate does appear to be slightly more reactive, and this is in accord with the difference in Free Energy (-1.5 Kcals/Mole) between the analogous 3-exo and 3-endo alcohols (31 and 42), derived from equilibration studies of the 7-exo-methylbicyclo(3,3,1)nonan-3-ols [26].

That both the 3-exo and endo tosylates are exceedingly reactive can be seen from Table 5 where relevant rate data has been collected. The relative rates of acetolysis of the 6-12 membered cyclanol tosylates have been correlated with the decrease in Internal (I) Strain associated with ionisation in the medium rings (8-11), where I-strain represents the total strain arising from compression of van der Waal's radii, distortion of bond angles and bond opposition forces [39]. The available data indicates that the medium rings are highly strained with the strain reaching a maximum in the 9-membered compound. Brown has found confirmation of this in the rates of reduction of the cyclic ketones with sodium borohydride, in the course of which a trigonal centre in converted into an approximately tetrahedral one with associated increase in I-strain: cyclodecanone was found to be the slowest of the medium-ring compounds in this context [40].

TABLE 5

ACETOLYSIS RATE DATA AT 25°C.

TOSYLATE	RATE CONSTANT (sec .)	k_{REL}	REF.
	5.82×10^{-5}	**1200**	-
	7.38×10^{-5}	**1500**	-
	9.25×10^{-5}	**1900**	-
cyclohexyl	4.88×10^{-8}	**1**	104
cycloheptyl	2.57×10^{-7}	**53**	39
cyclooctyl	2.82×10^{-5}	**580**	-
cyclononyl	2.43×10^{-5}	**500**	-
cyclodecyl	4.69×10^{-5}	**960**	-
cycloundecyl	6.03×10^{-6}	**120**	-
cyclododecyl	1.68×10^{-7}	**3**	-
	ca 5×10^{-8}	**1**	42
	2.01×10^{-7}	**4**	41
	4.87×10^{-7}	**10**	31
	5.32×10^{-7}	**110**	-

The rate enhancement found for the 3-exo and endo bicyclo(3,3,1)nonanyl compounds may be due wholly or in part to a similar relief of I-strain associated in the exo case with the deformations of the bicyclic ring system necessary to accomodate the specific $C_3 \ldots C_7$ transannular interaction and in the endo case with those arising from less specific interactions. This is supported by the fact that the rates of acetolysis of bicyclo(3,3,1)nonan-9-yl tosylate (64) [41] and 2-endo-bicyclo(3,3,1)nonanyl tosylate (54) [42] are of the same order as cyclohexyl tosylate, for in neither of these isomeric compounds is there the possibility upon ionisation of immediate refief of the I-strain, inherent in the bicyclo(3,3,1)nonane system.

The rate enhancement of the 3-exo and endo bicyclo-(3,2,1)-octyl tosylates (55, 56) are considered quantitatively compatible with the steric acceleration due to the ethane-bridge [31], more evident in the endo epimer since there is some relief of the steric crowding of the endo-hydrogens on the ethane bridge and the departing group in the transition state (57). The magnitude of the difference between the (3,3,1) and (3,2,1) 3 substituted bicyclic systems reflects the difference in inherent I-strain, or, some specific anchimeric effect, operative in the 3-exo and endo bicyclo-(3,3,1)nonanyl compounds.

The similarity in product distribution of 52 and 53

with that of cyclodecyl tosylate coupled with the similarly large relative rate constants may reflect a general trend, for, if the relief of I-strain is the dominant factor in each case, then elimination may be expected to be favoured over substitution since olefin formation incorporates two trigonal carbon atoms.

Experiments on bicyclo(3,3,1)nonan-3-one analogous to Brown's studies of the medium ring ketones have not yet been carried out, but the unreactive nature of this ketone had caused some perplexity, specifically with the attempted formation of the phenyl carbinol 58. All attempts to react the ketone with phenyl-lithium or phenyl magnesium halide were unsuccessful. Similar difficulties had been encountered during the attempted formation of the eneamine 59, although poor yields of the latter have been recorded [43]. Considering the rate of acetolysis (and extent of hydride shift, see later) and Brown's findings we would predict a marked increase in strain associated with addition reactions of the 3-ketone, and a destabilisation of intermediates of the type 60 (eg X = phenyl or morpholinyl).

The qualitative similarities of the bicyclo(3,3,1)nonane system with medium ring compounds noted in the introduction thus has a quantitative basis and the possible migration of hydride ion in the course of solvolysis demanded investigation. A feasible occurence in the course of

solvolysis of the 3-endo tosylate is a C_9,C_3 hydride shift (61) which might be expected to give rise to products derived from 62 or 63. The corresponding 9-tosylate (64) is known to produce four olefins (83%) and four acetates (17%) [41], outlined in scheme 1. thus the homogeneity of the olefin, identified as ^{2}-bicyclo(3,3,1)nonene, and the absence of detectable quantities of 9-alcohol or acetate in the products of acetolysis in both aqueous acetone and acetic acid is evidence against such a transannular migration.

In the course of solvolysis of the 3-exo tosylate the occurence of a C_7,C_3 hydride shift (66 to 68), analogous to a 1, 5 shift in an 8-membered ring, would be undetectable, unless the intermediate, 67, were possessed of unusual stability, in which event the interaction of solvent might be expected to furnish 3-exo substitution products in a highly stereospecific manner. The product analyses do not support the intervention of such an intermediate, but they afford little insight into the possibility of two cations as 66 and 68, co-existing via a higher energy transient species similar to 67, or the possibility of the migration of hydride concerted with ionisation (65, a+b). An investigation of such aspects required the use of isotopic labelling.

The simplest scheme which would differentiate products arising from 66 or 68 would require the formation of the monodeuterated alcohol 69, and whilst its epimer, 70, was readily accessible by lithium aluminium deuteride reduction, this

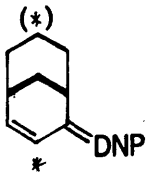
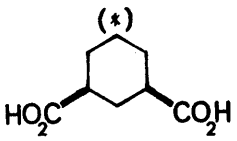
scheme was not utilised due to expected difficulties in the formation of 69. The tetradeutero-ketone (71) was available by a proton exchange, but it did not seem likely that the ketone could be reduced to the tetradeutero 3 exo alcohol without loss of deuterium, whereas the tetradeutero-endo alcohol (72) was readily prepared by hydride reduction. In hind-sight the exo-alcohols could probably have been obtained by inversion of the corresponding tosylates [44] of the more readily accessible endo-epimers.

A third possibility, utilising deuterium labelling, was investigated: C_7-deuterated compounds would be efficient in distinguishing products from 66 or 68, and would enable kinetic data to be obtained with respect to isotope effects, without the complications associated with deuterons on C_2 and C_4. A scheme was devised whereby the exomethylene-ketone 73 could be converted to the 7,7 dideutero-ketone 74, involving two specific lithium aluminium deuteride reductions (scheme 2). Thus the specifically labelled monodeuterated ketones 75 and 76 would also be available, and the C_3 carbonyl function could be modified at will, without interfering with the isotopic labelling. Unfortunately the conversion of 73 to 74 proved to be an inefficient synthetic route, due to side reactions more fully discussed in Section II. The prohibitively low yields of 74 prompted us to consider radioactive carbon labelling.

Of several synthetic routes to the bicyclo(3,3,1)nonane system, one of the most direct must surely be that discovered by Paul Rabe [45], who condensed acetoacetic ester with 3-methylcyclohexenone to produce 5-methyl-1-hydroxybicyclo-(3,3,1)nonan-3-one (77) directly. This route had attracted our attention and after modification of the reaction conditions, ^{2}-cyclohexenone could be converted to 1-hydroxy-bicyclo(3,3,1)nonan-3-one (78) in 56% yield. The replacement of the bridgehead hydroxyl group to give the bromo- or chloro-ketone (79) was facile and economical, for the bridgehead substituent was hydrogenolysed in the course of reducing the carbonyl function with lithium in liquid ammonia, to give 3-exo bicyclo(3,3,1)nonanol in fair overall yield. This synthetic scheme was clearly amenable to the incorporation of a C^{14}-isotope, by means of suitably labelled acetoacetic ester. Since the method of synthesis of commercial $3c^{14}$-acetoacetic ester ensures specific labelling [46], the product of condensation with cyclohexenone will be specifically labelled in position 3 (82, scheme 3), regardless of the sequence of intermediates involved in the Rabe condensation. It has not yet been established that hydrolysis and decarboxylation precede ring closure (ie. 83 may replace 81 in scheme 3). The conversion of the labelled ketol, 82, via the bromo-ketone to the $3C^{14}$ 3-exo alcohol, 84, would not interfere with the specific labelling pattern.

TABLE 6.

RADIOACTIVITY MEASUREMENTS : AQUEOUS ACETONE SOLVOLYSIS.

COMPOUND	RELATIVE MOLAR ACTIVITY (cpm/mM), Obsreved	Calculated
	3.75×10^4	ca 4.5×10^4
	-	ca 4.5×10^4
	4.31×10^4	ca 4.5×10^4
	2.74×10^2	-

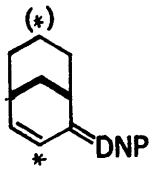
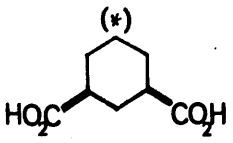
C^{14}-RETENTION OF 89 TO 88' : 0.64 %.

Solvolysis of the radioactive exo tosylate, 85, could conceivably give rise to two series of products differing only in the position of the isotopic carbon atom (scheme 4) derived from two cations related by a C_7, C_3 hydride shift. It is possible to distinguish between the C_3-and C_7-labelled olefins since these can be degraded to a compound containing 8 out of the 9 original carbons with the loss of C_3 specifically (scheme 5), to give cis-cyclohexane 1,3 dicarboxylic acid (89). The proposed degradation of the oxygenated solvolysis products (90, X = OAc or OH) proved unsatisfactory, (scheme 6) for the 3-ketone did not react with phenyl-lithium as noted above, precluding the oxidation of the phenyl carbinol to benzoic acid, (an excellent material from the stand-point of radioactive assay). A satisfactory alternative degradation has not been found, due in part to the low yield of substitution products from solvolysis reactions of this system.

In the event, the radioactive tosylate 85 was solvolysed in both aqueous acetone and acetic acid, and the olefinic product separated from the accompanying alcohols or acetates. The olefin resulting from solvolysis in aqueous acetone was oxidised in glacial acetic acid with selenium dioxide to the allylic acetate (87, X = AOc) which was in turn converted to the dicarboxylic acid (89) via the allylic alcohol (87, X = OH) and conjugated ketone (88). The Relative Molar

TABLE 7

RADIOACTIVITY MEASUREMENTS : ACETOLYSIS.

COMPOUND	RELATIVE MOLAR ACTIVITY (cpm/mM). Observed	Calculated
	7.0×10^4	ca 10^5
	-	ca 10^5
	9.96×10^4	ca 10^5
	3.55×10^3	-

C^{14}-RETENTION OF 89 RELATIVE TO 88' : 3.56 %

Activity (RMA) of the intermediates could not be accurately determined, due to their volatile nature, but the 2,4-Dinitrophenylhydrazone derivative of 88 was an ideal compound for radioactive assay. The results of this series are shown in Table 6. The olefin produced in acetolysis was oxidised in aqueous dioxane solution with selenium dioxide to furnish the allylic alcohol 87 (X = OH) directly [47]. The degradation was otherwise unmodified. The results of the acetolysis series are shown in Table 7.

The percentage of C^{14} isotope present in the final degradation product (89) represents the total extent of rearrangement occurring in each solvolytic medium and whilst alternative processes exist whereby C_7-labelled olefin may be produced, the most feasible is by C_7,C_3 transfer of hydride in the intermediate cation followed by elimination. Thus it seems reasonable to correlate the percentage C^{14} retention specifically with such a process although the final diacid 89 was not further degraded to locate the precise position(s) of the isotopic label. The results of 0.6% and 3.6% for the aqueous acetone and acetic acid solvolysis respectively, demonstrate an interesting decrease in hydride transfer in the more nucleophilic medium and preclude the possibility of significant C^{14}-scrambling in the course of degradation. Thus it would appear that transannular hydride shifts can in no way be considered major pathways in the course of kinetically

controlled solvolytic experiments in the 3 exo bicyclo(3,3,1)-nonanyl arene sulphonate system.

In view of the above findings, and those of Cope for the acetolysis of trans-5-methylcyclooctyl tosylate (see later)[48] it seems probable that a C_7,C_3 hydride shift does not occur to a significant extent in the course of solvolysis of 3-endo-bicyclo(3,3,1)nonanyl tosylate, however, no labelling studies have been conducted to establish this.

The very fast rate of reaction of the 3-exo tosylate can be attributed entirely to the relief of I-Strain in the course of ionisation, since significant transannular anchimeric assistance would be reflected in extensive re-arrangement of the C^{14} isotope in the above series of reactions. A similar finding may also apply to the 3-endo compound, in which case it is interesting that the accelerations arising from the relief of I-Strain, associated in the exo case with C_7,C_3 transannular crowding specifically, and in the endo case possibly with a boat ring and associated transannular effects are comparable.

Foote has shown that in certain cases the logarithm of the rate constant relative to cyclohexyl tosylate at 25°, is related to the stretching frequency of the parent ketone:

$$\log k = -0.132 \left(\nu_{c=o} - 1720 \right) \qquad \ldots(1)$$

Exceptions, however, are those reactions in which there

is anchimeric assistance or outside factors which affect the energy levels of the ground state and the transition state differently [49]. Estimates of the logarithm of the relative rate constant for the acetolysis of the 3 exo and 3 endo tosylates from equation 1, utilising a value of 1712 cm^{-1}. for the carbonyl stretching frequency of the 3-ketone (a weighted average of the two peaks at 1707 and 1717 cm^{-1}.), provide a value of log k = 1.05, which is in poor agreement with the observed values of 3.08 and 3.17 respectively. Clearly the 3-bicyclo(3,3,1)nonanyl compounds are exceptions.

Schleyer has equated the logarithm of the relative rate constant with three separate sources of strain:

$$\log k = (1715 - \nu_{C=O})/8 + 1.32 \sum_i (1 + \cos 3\theta_i) + (GS - TS)\ \text{strain}/1.36 \quad \ldots(2)$$

in which the first term is associated with Angle strain, the second with Torsional strain and the third with Non-bonded Interaction strain. This equation has been used to demonstrate the occurrence of anchimeric assistance in the course of certain reactions (as has equation 1) and to obtain a relative measure of this [50]. In the case of the 3 exo tosylate, each of these types of strain can only be estimated, but when reasonable values (see below) are incorporated, equation 2 accounts satisfactorily for the magnitude

of the observed relative rate constant and is evidence against anchimeric assistance.

Mean carbonyl absorption at 1712 cm. $^{-1}$ is probably an accurate reflection of the slight angle strain to be associated with the 3-ketone (or intermediate carbonium ion) but in all probability it is not indicative of the angle strain inherent in the ground state of either tosylate, in view of the localised transannular compressions being relieved upon ionisation. A better estimate of the angle strain present in the 3 exo tosylate may be obtained if the value of 1703 cm.$^{-1}$ is utilised (the stretching frequency of the 8 and 9 membered alicyclic ketones). Thus the first term of equation 2 has a value of 0.38-1.50.

The Torsional strain is dependant upon the angle , the average smaller torsional angle around each of the C-C bonds adjacent to the tosyl group, and is probably close to 60° or of the order of 50-60°, which affords a value of 0-0.36 for this strain component in equation 2. The Non-bonded Interaction strain associated with the C_3,C_7 transannular crowding may be of the order of 2 Kcals./Mole. (Schleyer has calculated a value of 1.8 Kcals/Mole for the total Non-bonded Interaction strain for the parent hydrocarbon bicyclo-(3,3,1)nonane [51].) If the transannular non-bonded interaction is totally removed in the transition state then the third term in equation 2 may be ca 1.45, and the sum equated

TABLE 8.

APPROXIMATE EXTENT OF HYDRIDE REARRANGEMENT IN ACETOLYSIS.

TOSYLATE	PERCENTAGE REARRANGEMENT		
	No Hydride Shift	Total Hydride Shift	Specific 1,5 Hydride Shift
cycloheptyl	96	4	-
cyclooctyl**	47	53	51
cyclononyl	70	30	20*
cyclodecyl	80	20	17*
cycloundecyl	90	10	9*
cyclododecyl	100	0	0

** brosylate[37]

* Due to the method of labelling,[38] the products from 1,4 and 1,5 hydride shifts cannot be distinguished, thus these approximate figures are inclusive and clearly represent the maximum values of 1,5 hydride shifts.

to 'log. k' can be seen to be of the order of 1.83-3.25 depending on the values incorporated. It is noteworthy that in the bicyclo(3,3,1)nonane system as the angle strain decreases an increase in the non-bonded interaction strain results, thus although the values noted above for each of these terms may individually be in error, it seems that their sum could reasonably account for a rate enhancement relative to cyclohexyl tosylate of the order of 10^3.

In the case of the 3-endo tosylate it is more difficult to estimate the individual strain components, however the observed rate enhancement is obviously compatible with that of its epimer, and there is no evidence to support anchimeric assistance, thus the source of acceleration may likewise be the relief of I strain.

The results obtained by Cope and Gale [37] in the acetolysis of the pentadeutero-cyclooctyl brosylate 91, are summarised in Table 8. The occurrence of almost exclusively 1,5-transannular hydride shifts has been elegantly demonstrated, and the extent of hydride rearrangement in the products, 53%, is a dramatic value when compared with our findings in a bridged cyclooctane system. An explanation for this difference which we find satisfactory is based on the reasonable supposition that transannular hydride shifts occur when the termini of migration are within a critical distance

of one another, and, disregarding for the moment the possibility of intermediates other than classical cations, an examination of Dreiding models (using the respective ketones as approximations) suggests that the 8 membered alicyclic ring is possessed of such greater freedom that a much closer approach of C_1 and C_5 is possible(92)than is permitted between carbons 7 and 3 in the bicyclic system.

The close approach of transannular centres, a possibility in all the medium rings (8-11) especially in the course of solvolytic reactions in which high energy transition states are involved, has been recognised for some time and the occurrence of hydride transfers has been demonstrated in a series of such compounds, by Prelog, utilising deuterium and C^{14} labelling. As can be seen from Table 8, the transannular transfer of hydride, in the course of acetolysis of the cyclanol arene sulphonate esters, attains a maximum in the 8 membered compound and is associated with a high specificity. Only in the 8 membered ring is hydride ion transferred in a 1,5 migration to the exclusion of all others, and to an extent which is outstanding when compared with the available data for the 9,10 and 12 membered compounds. A satisfactory explanation for this cannot be merely the possibility of close approach, but rather some favourable conformational force (or forces) present only in 8 membered ring, which serve to promote hydride specifically in a 1,5

manner. Whilst the ground state conformation of mono-substituted cyclooctane compounds is possibly heterogeneous [14], the high energy intermediate involved in acetolysis is in all probability unrestricted in this context, however there is present in the saddle and chair-boat conformations, transannular reflexes which may serve to place C_1 and C_5 in close juxtaposition.

In the saddle conformation, ionisation may be associated with the relief of transannular strain at C_1 and C_5, but the possibility exists of a balanced relief of strain of all four intra-annular hydrogen atoms. That is the reflex between C_3 and C_7 may operate as ionisation occurs or following ionisation, whichever, the effect is to balance the overall relief of transannular crowding by increasing the C_3,C_7 distance at the expense of the C_5,C_1 distance, and this may serve to place a hydrogen atom in an extremely favourable position for migration (9z).

A similar but less localised reflex effect may operate in the chair-boat conformation, which in the balanced relief of the crowding of the six intra-annular hydrogen atoms could place a C_5 hydrogen in the required proximity of the C_1 carbonium ion (94). Such balanced effects are not present in any of the other medium rings to the same extent, and are, of course, precluded by the introduction of a 3,7 methylene bridge across the 8 membered ring.

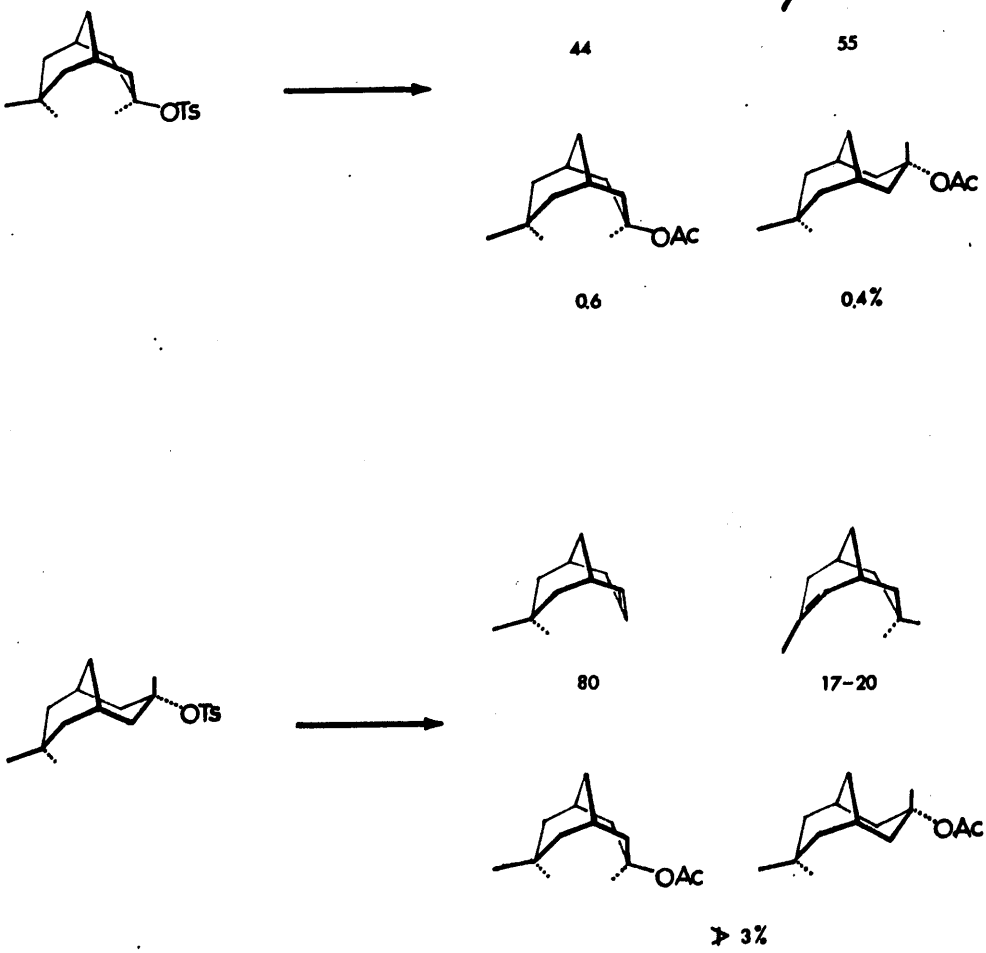
A bicyclic compound which promises to be of interest in this concept, is the substituted bicyclo(3,3,2)decane, 95, which may be subject to even greater steric acceleration than the corresponding bicyclo(3,3,1)nonanyl compound discussed above, for the two carbon bridge introduces additional strain which would be aleviated by ionisation at C_3 to produce an ion (96) with perhaps unique properties. The torsional effect of the two carbon bridge may place the C_7 endo hydrogen extremely close to the cationic centre at C_3 in the 'reflex' manner proposed above, in which case extensive hydride rearrangement might be expected, and if the process is concerted, some degree of anchimeric assistance.

Transannular hydride shifts have previously been recorded in the bicyclo(3,3,1)nonane system (see introduction), but no kinetically controlled experiments had been conducted to determine the extent and timing of the hydride migration relative to ionisation. In collaboration with Dr. S. Graham of Aberystwyth we investigated the related 7-exo-methylbicyclo(3,3,1)nonanyl compounds.

Preliminary product analysis on the acetolysis of 3-endo-7-exo-methylbicyclo(3,3,1)nonanyl tosylate(97), obtained as an oil, containing some 8-10% of its epimer (98), indicated that some transannular hydride migration occurs in the course

TABLE 9.

PRODUCTS OF ACETOLYSIS.



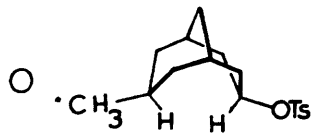
of solvolysis to the extent of 17-20% (Table 9). Kinetic data has not yet been obtained for this reaction, however.

Acetolysis of the 3-exo-7-exo-methylbicyclo(3,3,1)-nonanyl tosylate (98) proceeds slightly faster than the nor-methyl 3-exo tosylate (Table 4) and involved 55% trans-annular rearrangement, as evidenced by the products (Table 9). The products can be derived from the two cations 23 and 24, which have been shown to equilibrate, under thermodynamic conditions, to a 93% preponderance of the tertiary cation 24. That a 7,3 hydride shift occurs under kinetic control is of interest and raises the possibility of synchronous transfer, ie. the products could arise from interaction of the solvent with an intermediate similar to 100. If transfer of the hydride ion is concerted with the ionisation process, then the mono-deuterated tosylate 99, would be expected to show significant retardation in the rate of acetolysis relative to the nor-deutero compound (98).

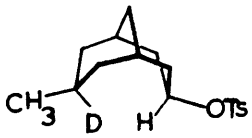
The synthesis of the specifically labelled tosylate (99) was facilitated by the availability of anti-3-endo-deutero-7-exomethylenebicyclo(3,3,1)nonan-3-ol (104), discussed more fully in Section II. Preliminary experiments on the unlabelled exomethylene alcohol 101, had produced a methyl ketone in very high yield, in a stereospecific manner 102, for the product was identical with authentic 7-exo-methyl-bicyclo(3,3,1)nonan-3-one (103). The corresponding conversion

TABLE 10.

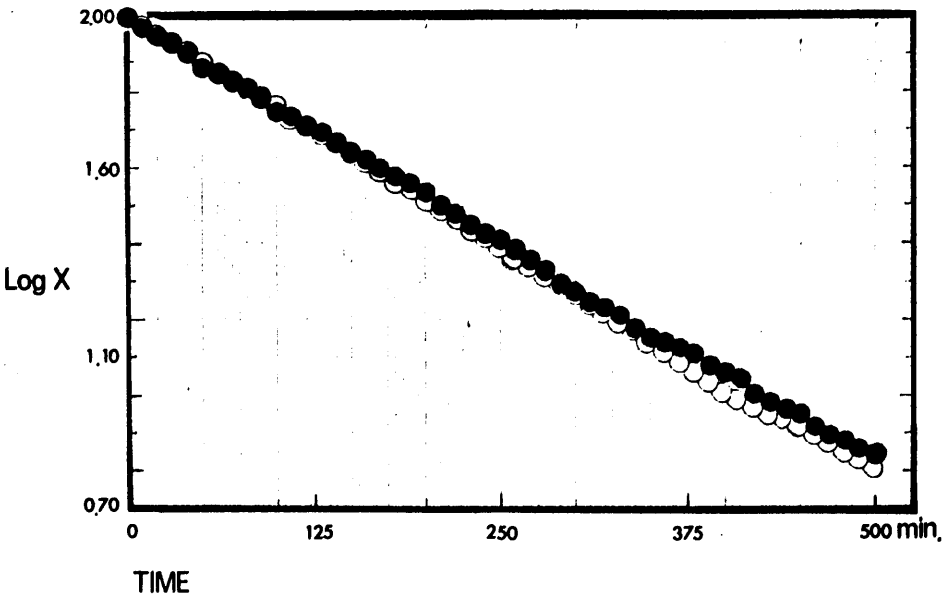
ISOTOPE EFFECT IN THE ACETOLYSIS OF **98** AND **99**.



$k_H = 9.25 \times 10^{-5}$ sec^{-1}.



$k_D = 9.25 \times 10^{-5}$ sec^{-1}.



Data from Appendix A, pages 106,107.

of the mono-deutero-alcohol 104, to the specifically labelled ketone 105, in the manner of Ayer and Piers [21], proceeded smoothly, and the location of the deuterium atom was established from the NMR spectrum. The formation of the monodeutero-3-exo alcohol (106) and the corresponding tosylate (99) were straightforward although the tosylate was a reactive crystalline solid,

The observed rate of acetolysis of the deutero-tosylate (99) was identical with that of the unlabelled tosylate (98), run simultaneously at 25°C (Table 10 and Appendix A) Thus in the absence of a detectable isotope effect (k_H/k_D = 1.00, within the limits of experimental error) it must be assumed that in the acetolysis of 3-exo-bicyclo(3,3,1)nonanyl arene sulphonates, transfer of hydride ion occurs after the rate-determining step. Whilst there is no appreciable stabilisation of the equivalent secondary cations (66 and 68), in the simple 3-exo case, this situation is unbalanced in the 7-exo-methyl-3-exo case, whereby a secondary cation is related to a tertiary cation via a hydride shift (23, 24).

Similar relative stabilities may account for the marked 1,5 transannular hydride rearrangement observed in the acetolysis of cis-5-methylcyclooctyl tosylate (90%), although the much lower figure observed for the trans compound (10%) favours the operation of some steric factor, or the operation of a concerted process in the cis compound. It is obvious

from these findings that the same classical cation cannot be involved to the same extent in both processes, thus the possibility of conformational forces determining the extent of hydride rearrangement seems attractive (108) and clearly could be involved in a fully concerted mechanism.

The question of the synchronous transannular transfer of hydride with ionisation in the solvolysis of the medium ring arene sulphonate esters has received little attention. Borcic and Prelog established the isotope effect operative in the acetolysis of 5,6 tetradeutero-cyclodecyl tosylate (110) relative to the non-labelled compound (k_H/k_D = 1.08) [52]. Unfortunately the method of introducing the deuteria may invalidate the results [53]. In view of the possibly unique properties of the 8-membered ring, an appraisal of the mode of transfer of hydride in the course of solvolysis seems justified, particularly in the light of Winstein's findings in the 'bird-cage' series of compounds. The brosylate 111, in which a nine-membered ring is severely constrained causing appreciable hydrogen congestion, was found to be 10^3 times more reactive in acetolysis than the corresponding 7-norbornyl brosylate (112, X = OBs), and the products indicate total transfer of hydride in the course of reaction, forming 113 (X = OAc) 83%, and 114 (X = OAc) 17%. Kinetic studies on the d_8-compound 115, revealed a significant decrease in rate, k_H/k_D = 1,24, and this is considered evidence of anchimeric

assistance associated with the hydride transfer,(116) [54]. Capon has suggested that the rate enhancement of 111 relative to 112 (X = OBs) is due to steric acceleration (relief of I-strain), there being less acceleration with the deuterated compound 115, because of the smaller steric requirements of deuterium [55], however our results indicate that where the rate enhancement is due entirely to the relief of I-strain the substitution of a deuterium atom (98, 99) does not lead to significant decrease in rate, and thus supports Winstein's interpretation.

Further investigations by Winstein in a related ring system (114, 117) are in progress. Preliminary results on the acetolysis of 117 (X = OTs) containing a severely strained 8 membered ring, indicate a relative activity some 10^5 times that of 7-norbonyl tosylate (112, X = OTs) producing the corresponding acetate (117, X = OAc), 80%, and an unidentified rearranged product, 20% [56]. The possibility clearly exists of appreciable involvement of hydride ion in the course of ionisation (118), and the relevant kinetic data and labelling studies will be of interest.

Thus the transannular transfer of hydride ion need not assist directly the process of ionisation, and appears to be associated with the close proximity of transannular centres, during the overall course of reaction, although 'unfavourable' shifts can occur under kinetic control when the energy

of the intermediate is thereby lowered. The requirements for transannular hydride shift are ill-defined and more data is required before the precise parameters are known.

EXPERIMENTAL

All melting points in this section were recorded on a Kofler block and are corrected, however the melting behaviour of bicyclo(3,3,1)nonanes is most unusual in that the collapse of the crystal into a mosaic takes place some 30 to 60 C^{o} below the temperature at which only liquid is present. Because of this and a marked dependence on the rate of heating, accurate and reproducable melting points are hard to obtain. It has been shown that inclusion of the material in a sealed capillary can raise the melting point in some instances to almost 200°C [57], and the agreement with melting points recorded in the literature is consequently poor.

The absorbants used for chromatography are commercial 'Woelm' alumina (basic or neutral). Light petrol refers to the fraction of b.p. 40 - 60° and petrol to the fraction of b.p. 60 - 80°. Thin-layer chromatoplates were prepared from Merck's'Kieselgel G' and were used under standardised conditions; solvent, 20% ethyl acetate-petrol, developed with ceric ammonium sulphate. The r_f-values quoted throughout refer to these conditions unless otherwise stated.

Analytical Gas-Liquid Chromatograms were obtained on a Pye-Argon Chromatograph using various columns. Retention Indices (R.I.) quoted throughout, refer to standard conditions

using a four foot analytical column, 10% Apiezon L. at 125°C with a gas flow of 50 mls/min. Additional GLC data is summarised in Appendix B. Temperature-programmed analytical GLC and Capillary GLC data were accomplished on a Perkin-Elmer F.11 instrument. Mass spectra were determined on an A.E.I. MS.9 spectrometer, except those denoted 'GCMS' which were obtained using a combined Gas-Liquid Chromatograph-Mass spectrometer, the LKB 9000.

Nuclear Magnetic Resonance (NMR) spectra were measured using carbon tetrachloride as solvent and tetramethylsilane as internal reference, unless otherwise stated; those denoted '60 Mc' were run on a Perkin-Elmer 60 Mc/sec. spectrometer, whereas those denoted '100 Mc' were recorded on a high resolution Varian 100 Mc/sec. spectrometer, with variable temperature facilities.

Routine infra-red spectra were measured on a Unicam S.P. 200 instrument; where high resolution is specified, spectra were recorded linearly in $cm.^{-1}$ as percentage transmission with a Unicam S.P. 100 double-beam infra-red spectrophotometer equipped with an S.P. 130 sodium chloride prism-grating double monochromator operated under vacuum. Ultra-violet absorption spectra were measured using an automatic Unicam S.P. 800 instrument, discussed more fully in Appendix A.

1-Hydroxybicyclo(3.3.1)nonan-3-one (78).

Ethyl acetoacetate (8.12g, 0.062M) and ^{2}-cyclohexenone (5g, 0.052M) were added to a solution of sodium (1.20g, 0.052M) in methanol (75mls.). The reaction was heated under reflux for 72 hours during which time the solution turned yellow and darkened progressively. A solution of potassium hydroxide (7.28g, 0.13M) in hot water (90 mls.) was added and the reaction again heated under reflux for a further 12 hours, then cooled.*

The basic aqueous solution was extracted once with an equal volume of ether (ca. 180 mls.), then with methylene chloride (3 x 180 mls.). The ether extract was kept separ- , washed once with dilute sulphuric acid (3N), then brine before it was dried (Na_2SO_4). The ethereal solution invariably contained methanol and other volatile compounds which were removed on a rotary evaporator to give a yellow oily solid, which produced a pale yellow solid on trituration with ether. Re-crystallisation from ether (at -10°C) furnished the desired product as an amorphous colourless solid (0.5g). The methylene chloride extracts were washed once with brine, dried (Na_2SO_4) and the solvent evaporated to give directly 1-hydroxybicyclo(3,3,1)nonan-3-one (78) as a colourless solid, which recrystallised from ether as amorphous crystals (4.0g, total yield 56%). m.p. 191-193°C, ν_{max} (high resolution, CCl_4) 3602, 1712, 1151, 1110, 1080 and 1007 cm^{-1}. Found; C 69.80, H 8.80 : $C_9H_{14}O_2$ requires;

C 70.10, H 9.15%. Mass spectral parent, 154. NMR (60 Mc): singlet @ 6.15 (1H, hydroxyl), sharp singlet @ 7.58 (3H), singlet @ 7.68 (2H), broad peaks @ 8.15 (3H) and 8.45 (5H).

* Low yields and solubility problems were encountered if there was deviation from these conditions, although the total yield was not markedly affected by change in the times of reflux, the durations given are those which optimised the yield.

1-Bromobicyclo(3.3.1)nonan-3-one (79, X = Br).

A solution of 1-hydroxy-3-ketone (78, 5.0g., 0.032 M) in ether (300 mls.) was added dropwise to a stirred solution of phosphorus tribromide (8.82g., 0.032 M) in ether (50 mls.). The cloudy yellow solution was refluxed for 1 hour, (during which time the ethereal solution cleared) then cooled, poured onto a dilute solution of hydrobromic acid (1 N) and ice and separated. The aqueous solution was washed with ether (2 x 50 mls.) and the combined ether solutions washed once with saturated sodium bicarbonate solution, brine, then dried (Na_2SO_4)

Removal of the solvent under reduced pressure at room temperature provided the highly crystalline bromo-ketone as a solid (6.8g, 97%), m.p. 83.5-84.5°C. Recrystallisation from pentane (twice at -10°C) gave colourless prisms of m.p. 84-85°C, with ν_{max} (high resolution, CCl_4) 1723, 1712 (inflexion), 1342, 1334, 1325, 1307, 1291, 1282, 1274, 1252, 1214, 1198, 1169, 1112, 1098, 1094, 1056, 1015, 973a, 950 and 920 cm^{-1}. Found; C 49.90, H 6.2[illegible]: $C_9H_{13}BrO$ requires: C 49.80, H 6.05%. Mass spectral parent ions, 216 and 218. NMR (60 mc), sharp singlet @ 6.92 (2H), sharp singlet @ 7.55 (6H), and broad peaks @ 7.72 (1H) and 8.3[illegible] (4H).

Endo-1-bromobicyclo(3.3.1)nonan-3-ol (80, X = Br)

A solution of the bromo-ketone (79, 4.5mM) in dry ether (50 mls) was added dropwise to a stirred slurry of lithium aluminium hydride (0.170g, 4.5mM) in ether (25 mls.) at room temperature, and the mixture stirred for 30 minutes. The excess hydride was destroyed by the careful dropwise addition of saturated sodium sulphate solution till the cloudy ethereal solution cleared and the insoluble inorganic salts settled. The ethereal solution was decanted and the residue dissolved in water (50 mls.) and extracted with ether (3 x 25mls.). The combined ether solutions were then washed once with dilute sulphuric acid (0.06 N), saturated sodium bicarbonate and finally brine, before being dried (Na_2SO_4).

Removal of the solvent furnished 3-endo-1-bromobicyclo (3,3,1)nonanol in excellent yield (96%) as a crystalline solid. Recrystallisation from pentane afforded fine prisms of m.p. 68-69°C, ν_{max} (mull) 3350, 1305. 1270, 1240, 1220, 1100, 1065, 1030, 980, 960, 900, 775 and 730 cm^{-1}. Found; C 49.75, H 6.90. $C_9H_{15}OBr$ requires; C 49.30, H 6.85%.

1-Chlorobicyclo(3.3.1)nonan-3-one (79, X = Cl).

Treatment of the 1-hydroxy-3-ketone (78) with phosphorus trichloride in ether in the manner described above produced the chloro-ketone in excellent yield. When phosphorus pentachloride was used the yields were lower. A solution of 1-hydroxy-3-ketone (78, 5g, 0.032 M) in ether (300 mls.) was added slowly to a stirred solution of phosphorous pentachloride (1g, 0.054 M) in ether (50 mls.), as before and the product isolated as described above (using HCl in place of HBr), as a pale yellow highly crystalline solid (6.0g) which decomposed unless immediately sublimed (at 120°C under atmospheric pressure). A further sublimation (at 80°C under 16mm. pressure) afforded 1-chlorobicyclo(3,3,1)nonan-3-one (3.25g, 57%) of m.p. 122-123°C with ν_{max} (high resolution, CCl_4) 1725, 1713, 1343, 1308, 1277, 1256a, 1233, 1217, 1201, 1171, 1113, 1096, 1058, 1018, 1006a, 973a, 956, 921, 879 and 871 cm^{-1}. Found; C 62.25, H 7.35: $C_9H_{13}ClO$ requires; C 62.60, H 7.55%. Mass spectral parent ions, 172, 173 and 174. NMR (60 Mc): sharp singlets @ 7.19 (2H), 7.62 , and 7.70 , the latter two overlapping broad peaks @ 7.5-8.0 (total integral 6H) and a peak @ 8.37 (5H)

Endo-1-chlorobicyclo(3.3.1)nonan-3-ol (80, X = Cl).

Lithium aluminium hydride reduction of 1-chlorobicyclo (3,3,1)nonan-3-one afforded the corresponding 3-endo alcohol (80, X = Cl) in excellent yield, as a glass-like solid which crystallised on standing. Recrystallisation from pentane resulted in highly crystalline prisms of m.p. 93-95°C, ν_{max} (mull) 3450, 1120, 1075, 1035, 985, 945, 910, 880, 810, 785, 770. and 745 cm^{-1}. Found; C 62.00, H 8.45: $C_9H_{15}ClO$ requires; C 62.00, H 8.65%

Acetylation Procedure

In this section, several acetylations of pure compounds, or of mixtures, were carried out. The acetylation procedure used, was identical in all cases and is described below using the preparation of 3-exo-bicyclo(3,3,1)nonanyl acetate (119) as an example. Careful control experiments showed it to cause no epimerisation in the systems examined.

To a solution of 3-exo-alcohol (30, 0.02g) in anhydrous pyridine (0.5 ml.) was added acetic anhydride (0.3 ml.) and the reaction left at room temperature for 12 hours. The solution was poured onto a dilute sodium bicarbonate solution (5 ml.), and extracted with pentane (3 x 5 mls.). The combined pentane extracts were washed with dilute sulphuric acid (0.6N. 5 mls.) saturated sodium bicarbonate solution (5 mls.) then brine (2 x 5 mls.) before being dried ($MgSO_4$). Careful evaporation of the solvent gave 3-Exo-bicyclo(3,3,1) nonanyl acetate as a colourless oil (0.21g) homogenous to TLC, ν_{max} (film) 1725, 1250, 1120, 1040, 980, 890 and 770 cm^{-1}. NMR (60 Mc): 9-line multiplet @ 4.62 (1 H, carbinyl J_{AX} = 11.0, J_{BX} = 6.0 c/s), sharp singlet @ 8.10 superimposed on broad resonance (5H), singlet @ 8.38 (6H) and broad resonance @ 8.50 (6H). The product was homogenous to GLC, R.I. 1335.

Acetylation provided a sensitive method of detecting epimeric impurities in this system, since the epimeric

3 exo and 3 endo alcohols (30, 39) could not be resolved on any of the available analytical columns, whereas the acetates were cleanly resolved.

3-Exo-bicyclo(3 3.1)nonanol (30)

(A) To a stirred solution of lithium (2.40g, 0.34M) in liquid ammonia (250 mls.) was slowly added a solution of dry t-butanol (25.3g, 0.34M) and 1-bromobicyclo(3,3,1) nonan-3-one (5.0g, 0.023M) in dry ether (50 mls.), over one hour. The liquid ammonia was maintained under reflux by means of an acetone-$CO_{2(s)}$ condenser, for a further three hours. Ether-methanol (1:1) was then slowly added till the blue colour of the liquid ammonia solution was discharged, then the condenser was removed and the ammonia allowed to evaporate, leaving a white solid mass, insoluble in the residual ether.

When the flask was at room temperature, dilute sulphuric acid (6N, 100 mls.) was added dropwise to the reaction flask, dissolving the basic white solid. The resulting two layers were separated and the aqueous phase was extracted with pentane (3 x 100 mls.). The combined ether-pentane solutions were then washed with brine (2 x 100 mls.) before being dried (Na_2SO_4).

Removal of the solvent produced a pale yellow amorphous solid (2.20g) which was not homogenous: TLC showed

2 spots of inequal intensity, the predominant compound had an r_f value of 0.35 and the impurity was much more polar, remaining at the origin. Chromatography or repeated recrystallisation from pentane afforded complete separation of the impurity (unidentified, but possibly polymeric) from 3-exo-bicyclo(3,3,1)nonanol obtained as colourless crystals (1.695g, 53%) of m.p. 96-97°C with ν_{max} (high resolution, CCl_4) 3630, 1475, 1045, 1005, 981, 955 and 917 cm^{-1}. Found; C 77.00, H 11.40: $C_9H_{16}O$ requires; C 77.10, H 11.50%. NMR (60 Mc): 9-line multiplet @ 5.68 (1H, carbinyl, X part of an A_2B_2X system with J_{AX} = 11.0 J_{BX} = 6.0 c/s), broad peak @ 8.00 (4H) with a sharp singlet superimposed @ 7.95 (hydroxyl proton), and a singlet @ 8.40 superimposed on broad resonance @ 8.50 (9H total).

A portion of the crude product was acetylated (as above) and GLC analysis indicated a very high stereospecificity in the product, (3 exo acetate 98%) there being less than 2% of the endo epimer present, and analysis of the alcohol after recrystallisation indicated that only the 3 exo epimer was present.

(B) Hydroboration of 2-bicyclo(3,3,1)nonene (27) according to the method of Lark [47], afforded in good yield a mixture of 2-exo and 3-exo bicyclo(3,3,1)nonanols (in 55:45 ratio respectively, by GLC analysis). Preparative TLC effected

a separation of the isomeric alcohols, and furnished 3 exo alcohol as colourless crystals (33%). GLC analysis (after acetylation) indicated high stereospecificity in the product, (3 exo epimer 95%). Recrystallisation from pentane afforded 3-exo-bicyclo(3,3,1)nonanol (30) as colourless needles of m.p. 94-96°C. Infra-red and NMR spectra were identical with these obtained for the alcohol produced above, as was the GLC behaviour of the alcohol and acetate.

(C) Sodium, moist-ether reduction of bicyclo(3,3,1) nonan-3-one (28) according to the method of Martin [24] (see section II) followed by chromatographic separation of the product from unreacted starting material furnished 3 exo bicyclo(3,3,1)nonanol in high stereospecificity (91%) as colourless crystals of m.p. 92 95°C. Recrystallisation from pentane afforded material with spectral properties identical with those of the products of the above two methods and showed consistent differences from the spectra of the 3-endo epimer.

3-Exo-bicyclo(3.3.1)nonanyl Toluene-p-sulphonate (52).

This preparation is typical of the tosylation procedure followed for compounds in this section. A solution of toluene-p-sulphonyl chloride (0.210g, 1.1mM) dissolved in the minimum amount of anhydrous pyridine was added to a solution of 3-exo alcohol (0.140g, 1.0mM) in minimum pyridine and the reaction maintained at 0°C overnight. The solution and deposited crystals were then poured into pentane (25 mls.) and the flask washed thoroughly with water (25 mls) and pentane (25 mls.). The aqueous solution was extracted thoroughly with pentane and the organic phase washed with dilute hydrochloric acid (2 x 25 mls, 0.1N) followed by saturated sodium bicarbonate solution (2 x 25 mls.) and brine (2 x 25 mls.) then dried ($MgSO_4$). Removal of the solvent under reduced pressure without heating afforded a colourless oil which could be readily crystallised at -10°C. Two recrystallisations from pentane at -10°C furnished 3-exo bicyclo(3,3,1)nonanyl-toluene-p-sulphonate (0.18g 60%) as colourless plates of m.p. 58-59°C, ν_{max} (mull) 1600, 1190, 1180, 1100, 940, 880, 855, 830, 740 and 680 cm^{-1}. NMR (100 Mc): an A_2B_2 quartet @ 2.34, 2.42, 2.79 and 2.87 (4H, Aromatic ring), a symmetrical 9-line multiplet centred @ 4.94 (1H, X part of an A_2B_2X system, J_{AX} = 11.0, J_{BX} = 6.0 c/s), sharp singlet @ 7.62 (3H, aromatic methyl) and complex methylene resonance from 8.00 to 8.6 (14H).

This tosylate was rather unstable in the solid state, and decomposed rapidly if heated past its melting point, and in a matter of days at room temperature. It could be kept for several days at 0°C. Its behaviour in solution, i.e. acetolysis followed an Arrhenius relationship with temperature as can be seen from the rate data in Appendix A.

3-Exo-bicyclo(3.3.1)nonanyl-p-Bromobenzonesulphonate

The corresponding 3-exo brosylate (52') was prepared in an analogous manner and provided an extremely reactive initially colourless crystalline product, of m.p. 56-57°C and ν_{max} (mull) 1580, 1190, 1110, 1100, 1075, 1020, 930, 870, 850 and 760 cm^{-1}. This material was extremely unstable, decomposing to a purple then black mass within 10-15 minutes of isolation at room temperature, and offered no advantages over the corresponding tosylate.

3-Bicyclo(3.3.1)nonanone (28).

(A) Oxidation of 3-exo alcohol derived from Birch type reduction of 1-bromobicyclo(3,3,1)nonan-3-one (79, X = Br), method A, see above, by Jones reagent [58] afforded a single ketone as a crystalline solid of m.p. greater than 136°C (sample sublimed from 125-136°C). Infra-red and NMR spectra were identical with those obtained for an authentic sample of Hall's ketone [57], assigned to the structure of 3-bicyclo (3,3,1)nonanone. The two ketones exhibited identical GLC behaviour. ν_{max} (high resolution, CCl_4) 2796, 1717, 1707, 1371, 1350, 1340, 1233, 1224, 1131, 1112, 1094, 955, 916 and 875 cm^{-1}. Found; C 77.90, H 10.05, $C_9H_{14}O$ requires; C 78.20, H 10.20%. NMR (60 Mc); a sharp singlet @ 7.65 (6H) singlet @ 8.18 (2H) and broad resonance @ 8.38 (6H). The mass spectrum was identical with that of Hall's ketone, parent ion 138.

(B) Jones oxidation of the 3-exo alcohol derived from hydroboration of ^{2}-bicyclo(3,3,1)nonane (27) method B above, has been shown to give 3-bicyclo(3,3,1)nonanone (28) identical in all respects with Hall's ketone [43].

(C) Preliminary hydrogenation studies of the bromo-ketone (79) indicate a possible alternative synthesis. A suspension of 1-bromobicyclo(3,3,1)nonan-3-one (0.078g), fused sodium acetate (0.290g) and palladium-calcium carbonate

catalyst (1%; 0.320g) in ethanol (15 mls.) were hydrogenated at room temperature. Hydrogen uptake (theoretical amount) took 5 hours, when the reaction was worked up according to the method of Cope [48], to yield a colourless solid in good yield (ca 0.05g) with ν_{max} (film) 1740, 1710, 1380, 1350, 1290, 1230, 1200, 1150, 1110, 1080, 945, 800 and 780 cm^{-1}. TLC showed only one spot, but this was not meaningful since starting material and 3-bicyclo(3,3,1) nonanone had the same r_f value. GLC was much more informative and indicated the presence of 3 compounds in the crude product; the main peak (ca 80%) had the same retention time as authentic 3-bicyclo(3,3,1)nonanone, (R.I. 1235), whereas the other two compounds (R.I. 1450 and 1480) were comparable with starting material (R.I. 1480).in molecular weight/volatility and hence may both be bromo-ketones.

A more detailed investigation of this reaction is warranted since it may represent an excellent route to the nor-bromo 3-ketone (28), however the reaction products were not further characterised.

(D) See section 11.

3-Bicyclo(3.3.1)nonanone
p-Bromobenzonesulphonylhydrazone

The heavy-atom derivative was prepared in the usual manner. Recrystallisation from ethanol afforded crystals of m.p. 165-166°C (d) which were not suitable for X-ray crystallographic study. ν_{max} (mull) 3250, 3010, 1580, 1375, 1280, 1180, 1090, 1070, 1040, 1015, 970, 940, 925, 835, 800, 875 and 850 cm^{-1}.

2.2.4.4.Tetradeutero-bicyclo(3.3.1)nonan-3-one (71)

In the manner of Schaeffer and Lark [64] bicyclo (3,3,1) nonan-3-one (0.20g, 1.45mM) was dissolved in dioxane (5mls, spectroscopic grade) then transferred to an ampoule, D_2O (5 mls) and sodium (ca 20 mg.) were added and allowed to react before the ampoule was sealed and maintained at 95°C for 14 days. It was then removed, cooled and the contents poured into pentane (100 mls). The organic phase was washed with ice-cold water (5 x 50 mls), dried ($MgSO_4$), the solvent carefully removed under reduced pressure and the product obtained sublimed to furnish a colourless crystalline solid ν_{max} (high resolution, CCl_4) 2918, 2873, 2848, 2209, 1705, 1468, 1457, 1443, 1266 and 1137 cm^{-1}. NMR (60 Mc) 3 groups of peaks as in 3-bicyclo(3,3,1)nonanone @ 7.65 (2H), 8.18 (2H), and 8.40 (6H), consistent with -proton exchange. Mass spectral analysis indicated

a parent ion m/e 142 (ca 45% of base peak); p + 1 ion (8%); p - 1 ion (8%); which compares with mass spectrum of the starting ketone (24), parent ion 138 (ca 38%), p + 1 (6%), p - 1 (7%); and the incorporation of only 4 deuterium* atoms

* It was considered expedient to check that in bicyclo(3,3,1)nonan-3-one a potential deuterium label at C_7 would not be exchanged in the course of basic reduction (lithium/liquid ammonia) and the finding of only 4 deuteria in the product above preclude this possibility.

3-ENDO-bicyclo(3.3.1)nonanol (39).

Lithium aluminium hydride reduction of 3-bicyclo(3,3,1) nonanone (28) in the manner previously described, produced a crystalline alcohol in excellent yield. Recrystallisation from pentane afforded material apparently homogeneous to TLC and GLC analysis. The infrared and NMR spectra were different from those of 3-exo-bicyclo(3,3,1)nonanol (see below). Since this alcohol could also be readily oxidised to 3-bicyclo(3,3,1)nonanone it was assigned the epimeric endo structure (39). GLC analysis of the crude product after acetylation indicated that the hydride reduction had occurred with high stereospecificity to furnish at least 90% of the 3 endo epimer. Recrystallisation from pentane failed to remove entirely the epimeric 3 exo alcohol (after 6 recrystallisations there was still some 4% 3 exo epimer present according to GLC analysis after acetylation) however, it afforded 3-endo-bicyclo(3,3,1)nonanol as colourless needles of m.p. 122-123°C, ν_{max} (high resolution, CCl_4) 3623, 1468, 1110, 1056, 1022, 1012, 962 and 931 cm^{-1}. Found; C 76.80, H 11.50: $C_9H_{16}O$ requires; C 77.10, H 11.50%. NMR (60 Mc). An asymmetric multiplet centred @ 6.12 (1H, carbinyl) a complex pattern @ 7.88 (4H), a sharp singlet @ 8.32 (1H, hydroxyl) and complex series of peaks from 8.50 to 9.02 (10).

3-ENDO-bicyclo(3.3.1)nonanyl Acetate (120).

Several samples of the 3-endo alcohol (39) were recrystallised sequentially from pentane then acetylated as described above, to afford an oil homogeneous to TLC with ν_{max} (film) 1725, 1250, 1150, 1110, 1055, 1035, 970, 900, 855, 800, 760 and 715 cm^{-1}. GLC analysis showed the product to be 3-endo-bicyclo(3,3,1)nonanyl acetate (R.I. 1360) accompanied by some 4-9% 3-exo-bicyclo(3,3,1)nonanyl acetate (R.I. 1335).

3-ENDO-bicyclo(3.3.1)nonanyl Toluene-p-sulphonate (53)

The tosylate ester was prepared from 3-endo alcohol (39) as described above, but all attempts to induce crystallisation failed and the product remained in our hands as a pale green oil, which proved to be impossible to purify due in part to the reactivity of 3-endo-bicyclo-(3,3,1)nonanyl tosylate (53), ν_{max} (film) 1600, 1300, 1190, 1180, 1100, 940, 870, 840, 820, 710 and 680 cm^{-1}. NMR (100 Mc). An A_2B_2 quartet @ 2.33, 2.41, 2.78 and 2.86 (ca 4H, aromatic ring), a 7-line multiplet centred @ 5.45 (ca 1H, X part of an A_2B_2X system, J_{AX} = 7.0, J_{BX} = 14 c/s) sharp singlet @ 7.62 (ca 3H, aromatic methyl) and complex methylene resonance from 7.98 to 8.80 (ca 14H). The integration was complicated by the presence of residual solvent and trace impurities.

3-ENDO-bicyclo(3.3.1)nonanyl p-Bromobenzonesulphonate.

The product was obtained in an analogous manner as an extremely reactive oil, which resisted all attempts to induce crystallisation, ν_{max} (film) 1580, 1185, 1100, 1075, 1020, 930, 875, 850, 835, 770, 755 and 710 cm^{-1}.

Solvolysis of 3-EXO-bicyclo(3.3.1)nonyl-p-toluenesulphonate (52).

3-Exo-Tosylate (0.93g, 3.16mM) was added to a suspension of lithium carbonate (0.129g 1.74mM) in 80% aqueous acetone (31.6 mls), the flask stoppered and maintained at 50°C for 96 hours. The mixture was cooled, poured onto pentane (150 mls) and the organic layer washed with water (5 x 30 mls) then dried (Na_2SO_4) before the solvent was removed under reduced pressure. The resulting colourless oil (0.380g) could readily be crystallised at 0°C but was mobile at room temperature. TLC indicated only 2 spots, corresponding to olefinic product(s) (r_f 1.00, stain:pink) and alcoholic products (r_f 0.30, stain: blue-green). The infra-red spectrum was indicative of a mixture of alcohol(s) and ^{2}-bicyclo(3,3,1)nonene with a vast preponderance of olefin.

The total solvolysis products were dissolved in light petrol and made up to 10 mls in a graduated flask. This solution was used for GLC analysis, which showed only two peaks corresponding to a mixture of ^{2}bicyclo(3,3,1)nonene and 3-bicyclo(3,3,1)nonanols. (The olefin was found to give

a single peak of identical retention time to that of authentic ^{2}-ene under a wide variety of GLC conditions).

The ratio of olefin: alcohol(s) was established by comparison with a standard solution. 3-EXO alcohol (2.40 mgs) was dissolved in 2.0 mls of light petrol (conc. 1.2 g per 1). It was found that a 5 l injection consistently produced a peak of area 0.574 sq. ins. (equiv. to 6.0 g). Thus the peak area represented 10.48 g./sq.ins. 3-EXO alcohol. It was found that a 2.0 l injection of the standard solvolysis product solution produced a peak of area 0.660 sq. ins. This implies a concentration of 34.5 mgs. of 3-alcohol in the 10 ml solution or 9.08% of the total solvolysis product, (assuming equal detector response for each epimer, which later experiments were to indicate as most probable.)

A portion of the total solvolysis products was acetylated and GLC analysis of the acetates produced indicated that only the 3-EXO and 3-ENDO acetates (119,120) were present, in the ratio of 40 : 60 (average of 5 Runs, all in good agreement).

Solvolysis of 3-ENDO-bicyclo(3.3.1)nonyl-p-toluenesulphonate.(53).

3-ENDO-Tosylate (1.66g 5.65mM), obtained as an oil, contaminated by 9% of its epimer, was solvolysed in 80% aqueous acetone (56.5 mls) containing lithium carbonate (0.46 g, 6.22mM) for 168 hours in the manner described above.

The colourless oil produced (0.60g) was shown to be a mixture of the same three products. A portion (0.05g) was again acetylated and the ratio of 3 EXO to 3 ENDO acetate (119, 120) was found to be 68 ; 32. The remainder (0.55g) was chromatographed on grade IV alumina. Elution with light petrol afforded the olefin (0.369g 72.8%) and elution with 20% ether-petrol furnished the alcohols (0.138g 27.2%).

GLC analysis and comparison infra-red spectra again indicated that the olefin was identical with authentic ^{2}-bicyclo(3,3,1)nonene. A portion (0.01g) of the chromatographed alcohols was acetylated and GLC analysis confirmed the mixture of only 3 EXO and 3 ENDO acetates (the ratio 72.6 : 27.4). A mean value was used to calculate the product distribution. A correction can be made for the presence of 9% of the epimeric tosylate in the starting material.

Acetolysis of 3-EXO-bicyclo(3.3.1)nonyl Toluene-p-sulphonate. (52)

A solution of 3-EXO-tosylate (0.345g, 1.17mM) and fused sodium acetate (0.106g, 1.29mM) in anhydrous acetic acid (12 mls) was thermostated at 50°C for 12 hours. The reaction was cooled and the contents poured onto pentane (50 mls). Solid anhydrous sodium carbonate was added slowly, then brine (25 mls), and sufficient sodium carbonate solution was added to bring the pH of the aqueous solution to 5. The resulting aqueous phase was extracted twice with pentane (50 mls) and the combined extracts were washed with dilute sodium bicarbonate solution (1 x 50 mls), then brine (1 x 50 mls) before being dried ($MgSO_4$). The bulk of the solvent was removed under reduced pressure, but the last traces were allowed to evaporate at atmospheric pressure. The product, a colourless oil (0.120g) had characteristic infra-red absorption at 3050, 1650 and 710 cm^{-1}. which was more intense than that at 1725 and 1250 cm^{-1}, which suggested that the ratio of olefin to acetates might be very high.

GLC analysis supported this in that the major product was an olefin of identical retention time with that of ^{2}ene (27), and the acetates produced were identified as 3-exo and 3-endo epimers in the ratio of 60 ; 40 (This ratio was substantiated by a number of self-consistant runs.)

Chromatographic separation of the acetolysis products of a later run was achieved on grade III neutral alumina. Elution with pentane furnished the olefin (267 mgs, 95%) and elution with 5% ether-pentane, the acetates (14 mgs, 5%). The olefin thus obtained was shown to have identical infra-red absorption with that of Δ^2-bicyclo(3,3,1)nonene: ν_{max} (high resolution CCl_4) 3058, 3022, 1648, 1461, 1451, 1441, 1428, 1327, 1196, 1158, 1007, 924 and 887 cm^{-1}.

Acetolysis of 3-ENDO-bicyclo(3.3.1)nonyl-p-toluenesulphonate. (53)

A solution of 3-ENDO-Tosylate * (0.370g, 1.25mM), and fused sodium acetate (0.114g, 1.38mM) in anhydrous acetic acid (12.5 mls) was thermostated at 50°C, for twelve hours. Work up, as before produced an oil (approx. 0.10g) with infra-red absorption at 3050, 1650 and 710 cm^{-1} of intensity comparable with that at 1725 and 1250 cm^{-1} indicating predominance of olefin formation. GLC analysis supported this and indicated that the olefinic product was one peak and compatible with Δ^2-bicyclo(3,3,1)nonene under the standard conditions in use.

The ratio of olefin to acetates (91 : 9) was obtained by peak area measurement and assumes equal detector response to olefin and acetates. The ratio of epimeric acetates was found to be somewhat variable although measurements taken from the final three runs ‡ were consistant at 70 : 30 3 EXO : 3 ENDO (119 : 120).

* as a colourless oil containing 9% epimeric tosylate.

‡ solvolysed at 80°C. The acetates and olefin have been individually subjected to the solvolysis conditions of buffered acetic acid at 80°C for periods up to a week without undergoing any change.

2-Bicyclo(3.3.1)nonene (27).

To a solution of sodium (2.84g, 0.123M) in diethylene glycol (100 mls) was added hydrazine hydrate (100% ; 10 mls) and 2-bicyclo(3,3,1)nonen-9-one (5.60g, 0,041M), and the mixture was heated under reflux for 1 hour, during which time a white crystalline material collected in the condenser. The infra-red spectrum of this compound was compatible with a hydrazone derivative. The crystalline intermediate was washed down the condenser with ether (which refluxed continuously). The temperature of the heating bath was raised so that a vigorous reflux was maintained for 7 hours, (the volatile nature of the intermediate hydrazone derivative precluded the distillation of unreacted hydrazine).

The solution was then distilled till the temperature of the reaction flask reached 210°C. The two layer distillate was extracted with pentane (4 x 40 mls), and the combined organic phase was washed with dilute hydrochloric acid (6N) till free from base, then with water (3 x 50 mls) then dried

($MgSO_4$). Careful removal of the solvent, without heating, under reduced pressure afforded a colourless oil which was found to be extremely volatile, but was not homogeneous to TLC. Chromatographic purification of the olefin on grade I (neutral) alumina afforded a colourless low-melting solid (4.0g, 77%) which was homogeneous to TLC and GLC, but which contained residual solvent, Sublimation afforded 2-bicyclo(3,3,1)nonene (28) as a wax-like solid of m.p. 96-98°C (Literature 96-100°C [41]), ν_{max} (high resolution CCl_4) 3058, 3022, 2930a, 2904, 2879, 2854, 2833, 1648, 1461, 1451, 1441, 1428, 1327, 1196, 1158, 1007, 924 and 887 cm^{-1}. Found; C 88.20, H 11.40. C_9H_{14} requires; C 88.45, H 11.55% NMR (60 Mc). A degenerate AB signal @ 4.13 and 4.38 (2H, with greater multiplicity associated with the latter signal, hence C_2-H and C_3-H respectively) broad complex resonance from 7.60 to 8.10 (6H) and a broad double peak centred @ 8.50 (6H)

Allylic oxidation of ^{2}-bicyclo(3.3.1)nonene (Scheme 5).

(a) The olefin (0.750g, 6.15mM) was added to a suspension of selenium dioxide (0.450g, 4.0mM) in acetic anhydride (0.25 ml) and glacial acetic acid (7.0 mls) and the mixture refluxed for 90 minutes. The solution turned red, then darkened. The reaction was cooled, diluted with pentane (50 mls) then filtered free from selenium residues. The pale yellow filtrate was washed with a saturated sodium bicarbonate solution (2 x 25 mls), then with brine (3 x 25 mls), dried ($MgSO_4$), and the solvent evaporated at reduced pressure. The viscous yellow oil (0.810g, 73%) was homogeneous according to TLC (r_f - 0.50, stained sky-blue whereas the starting olefin, r_f 1.00, stained pink) and to GLC (suggesting stereospecific oxidation.) The I.R. spectrum (film) ν_{max} 3015, 1725, 1370(s), 1240(s), 1170, 1125, 1050, 1030, 1020, 990, 970, 955, 930, 875, 860, 795, and 750 cm^{-1}. was compatable with the allylic acetate (87, X = OAc)

Hydrolysis of the acetate was affected by dissolving the ester (0.810g, 4.5mM) and sodium hydroxide (0.40g, 10mM) in aqueous methanol (1:1, 15 mls), and maintaining the solution at reflux for 3 hours. When cold, the solution was diluted with brine (30 mls) and extracted with pentane (3 x 30 mls). The organic phase was separated, washed with dilute sulphuric acid (0.1N, 20 mls) saturated sodium bicarbonate solution (25 mls) and brine (3 x 25 mls), dried (Na_2SO_4)

Then the solvent was removed at reduced pressure. The yellow semi-solid produced could be readily purified by sublimation or chromatography to give a colourless solid in good yield, homogeneous to TLC (r_f 0.20, stained: blue). TheI.R. spectrum (film) $_{max}$, 3400, 3050, 2700, 1650, 1160, 1120, 1050, 1035, 1100(a). 900, 880, 850, 825, 790 and 750 cm^{-1}. was compatible with the expected product ^{3}bicyclo(3,3,1)nonan-2-ol (87, X = OH) [47].

(b) The allylic alcohol could be obtained directly from the olefin according to the procedure of Lark [47].

2-Bicyclo(3,3,1)nonene (1.675g, 13.7mM) was dissolved in distilled dioxane (20 mls), and water (3 mls), followed by selenium dioxide(1.7g, 15.3mM) was added and the solution refluxed for 24 hours. The solution was cooled, filtered free from selenium residues, dissolved in pentane (150 mls) and washed with brine (2 x 30 mls) then water (4 x 30 mls). The pale yellow pentane solution was dried (Na_2SO_4) and the solvent removed under reduced pressure, to furnish a yellow oil. TLC indicated th presence of the allylic alcohol (r_f 0.20, stained: blue) and a less polar compound (r_f 0.90) as a yellow spot, visible before and after staining.

A chromatographic separation was readily achieved and the yellow oil (o.4g) was set aside. The allylic alcohol (0.808g, 43%) was obtained as a crystalline solid, m.p. 98 - 100°C, with an infra-red spectrum identical with that

obtained by the previous route. Literature m.p. 103 - 103.5°C [47].

A later study of the less polar oil, thought to be an intermediary selenate ester, suggested that it had disproportionated to the allylic alcohol and a dark-red precipitate of selenium dioxide, but time did not permit of the collection of data, to confirm this.

^{3} Bicyclo(3.3.1)nonen-2-one (88).

Jones oxidation of ^{3}bicyclo(3,3,1)nonan-2-ol (0.80g, 5%mM) at 0°C afforded the expected product (88) in good yield. The enone was purified by sublimation at 100°C and atmospheric pressure, to provide ^{3}bicyclo(3,3,1)nonen-2-one as colourless crystals (o.68g, 58%), of m.p. 96 - 98°C (literature value 97.5 - 98.5°C [47]), ν_{max} (mull) 3050, 1675, 1465, 1385, 1315, 1245, 1200, 1135, 1080, 895, 830 and 730 cm^{-1}.

The corresponding 2;4 dinitrophenylhydrozone was prepared according to the method of Braidee [60] and afforded fine dark red needles after two recrystallisations from methanol of m.p. 203 - 204°C. Found; C 57.05, H 4.95, N 17.35. $C_{15}H_{16}O_4N_4$ requires; C 56.95, H 5.10, N 17.70%

Permanganate Oxidation of ^{3}Bicyclo(3.3.1)nonen-2-one.

The method was that of Martin [24], the unsaturated ketone (88, 0.10g) was dissolved in acetone (7 mls) at room temperature, and a solution of potassium permanganate in dilute sulphuric acid (2.5g/100 mls N acid) was slowly added with stirring till a permanent pink colour remained above the heavy precipitate of manganese dioxide. The solution was then filtered through 'Celite 535' and the flask and filter washed with ethyl acetate. The aqueous filtrate was extracted with ethyl acetate (3 x 30 mls) and the combined ethyl acetate solutions washed once with brine (20 mls). The organic layer was then extraced with saturated sodium carbonate solution (3 x 30 mls). The ethyl acetate solution was washed once more with brine, dried (Na_2SO_4) and the solvent removed on a rotary evaporator to give the neutral products (5mgs) which were not identified.

The basic carbonate extracts were identified with sulphuric acid (12 N) and re-extracted with ethyl acetate (4 x 50 mls). The organic phase was washed with brine (50 mls) and dried (Na_2SO_4). Removal of the solvent furnished the acidic products (30 mgs) as a yellow solid. Recrystallisation from ether afforded a colourless solid of m.p. 159 - 162°C, ν_{max} (mull) 3100 (broad), 1705, 1380, 1330, 1300, 1290, 1215, 1190, 1130, 955, 920 and 745 cm^{-1}.

Found; C 56.25, H 6.80. $C_8H_{12}O_4$ requires; C 55.80, H 7.00 %. The literature values of the m.p. of the cis and trans cyclohexane-1,3-dicarboxylic acids are respectively 167°C and 150°C, [61] and a value of 150 - 155°C has been reported for the mixture of the two acids produced on catalytic hydrogenation ofiscphthalic acid (ca 50 - 60% cis),[62] thus it would appear that some epimerisation has occurred in the course of work up, for the product cis-cyclohexane-1,3-dicarboxylic acid (89) has infra-red spectral absorption very similar to the product obtained by catalytic hydrogenation as above.[63]

Attempted formation of 3-Phenylbicyclo(3.3.1)nonan-3-ol (58)

A. A solution of bicyclo(3,3,1)nonan-3-one (1.00g, 7.15mM) in ether (30 mls) under nitrogen was added to a cooled solution of phenyl lithium under nitrogen prepared from bromobenzone (1.0 ml, 10mM) and lithium (0.15g, 21mM) in ether (10 mls) and filtered free from excess lithium. The reaction was stirred at room temperature for 3 hours under nitrogen then worked up, in the manner of Leete[65]. Only unreacted 3-ketone was obtained.

The reaction time was increased to 6 hours without effect. A 5 molar excess of phenyl lithium was used and the reaction time increased to 12 hours without effect. A similar reaction in light petrol-ether (1 ; 3) was maintained

at reflux for 15 hours without forming the required phenyl carbinol (58), but a hydrocarbon produced in poor yield was obtained as a colourless crystalline solid and was identical in all respects with an authentic sample of diphenyl.

B. A solution of bicyclo(3,3,1)nonan-3-one (1.15g, 8.2mM) in ether (50 mls) was added to a solution of phenyl magnesium bromide, prepared in the usual manner [66] from magnesium (1.00g, 41mM) and bromobenzene (4.5 mls, 43mM) in ether. (A portion of the grignard solution was tested by bubbling in CO_2 gas and successfully isolating benzoic acid). The reaction was stirred at room temperature for 2 hours, then maintained at reflux for a further 10 hours. Routine work-up afforded unreacted 3-ketone and no hydroxylic product.

Synthesis of C^{14}-labelled compounds

Series A.

3-C^{14}-1-hydroxybicyclo(3.3.1)nonan-3-one (82).

Commercially available 3-C^{14}-acetoacetic ester (0.1mc) of high specific activity, 1.26 x 10^{10} counts per minute/millimole, was diluted with unlabelled acetoacetic ester to 8 mls (8.12g). The radioactive ester, of specific activity 3.54 x 10^{6} cpm/mM, was condensed with cyclohexenone in the usual manner to provide pure 3-C^{14}-1-hydroxybicyclo(3,3,1)nonan-3-one (3.0g after recrystallisation)

The radioactivity of the product was measured on an anti-coincidence counter of 5-6% efficiency. The mean experimental value of 1.76 x 10^{5} cpm/mM for the relative molar activity is in agreement with the calculated value, 1.7 - 2.1 x 10^{5} cpm/mM (5 - 6% of 3.54 x 10^{6} cpm/mM).

3-C^{14}-3-EXO bicyclo(3,3,1)nonanol (84).

The radioactive hydroxy-ketone (3.00g) was diluted with unlabelled hydroxy-ketone (1.00g) and treated with phosphorus tribromide in ether, as before, to obtain 3-C^{14}-1-bromobicyclo (3,3,1)nonan-3-one in 96% yield (5.45g).

The bromo-ketone was reduced with lithium in liquid ammonia and the crude product chromatographed, then recrystallised to furnish 3-C^{14}-3-EXO bicyclo(3,3,1)nonanol

(1.236g, 35%). The radioactivity was measured as above, but was found to fall off with time in a fairly linear fashion and this was attributed to the volatile nature of the alcohol. Five counts were obtained at 1 hour intervals and if plotted against time can be seen to make an intercept at zero time of 10100 (counts in 3 Ksec.) corresponding to an instantaneous rate of 202 cpmin. and a value of approximately 10^5 cpm/mM. for the relative molar activity, in fair agreement with the expected value of 1.32×10^5 cpm/mM.

3-C^{14}-3-EXO-bicyclo(3.3.1)nonyl-p-toluenesulphonate (85).

Radioactive 3-EXO-alcohol (0.35g, 2.5mM) of relative molar activity approx. 1.32×10^5 cpm/mM was diluted with unlabelled 3-EXO alcohol (0.65g, 4.64mM), dissolved in pyridine (minimum) and treated with a solution of p-toluenesulphoryl chloride (1.50g, 7.86mM) in pyridine, and the reaction worked up as previously described. The crude solid tosylate ester was recrystallised twice from pentane to give fine plates (1.32g) of m.p. 58-59°C.

The relative molar activity was found to be 3.75×10^4 cpm/mM which was rather lower than anticipated (4.62×10^4 cpm/mM), but due to the inherent liability of this compound to decomposition this was considered adequate agreement.

Solvolysis of $3C^{14}$-3EXO-bicyclo(3.3.1)nonyl-p-toluenesulphonate.

The radioactive tosylate (1.316g, 4.47mM) and lithium carbonate (0.366g, 4.94mM) were added to 80% aqueous acetone (45 mls) and the reaction maintained at 50°C for 96 hours. The reaction was worked up as before, the solvolysis products separated and the radioactive olefin thus obtained degraded.

Degradation of C^{14}-labelled 2-bicyclo(3.3.1)nonene (86).

The radioactive olefin (0.5g), from aqueous acetone solvolysis of $3C^{14}$-3EXO tosylate, selenium dioxide (0.30g, 2.7mM) and acetic anhydride (0.1 ml) were heated in glacial acetic acid (10 mls) to form the allylic acetate (87, X = OAc), as before.

The allylic acetate (0.7g) was hydrolysed in refluxing aqueous methanol (1:1, 15 mls) containing sodium hydroxide (0.4g, 10mM) to produce the radioactive allylic alcohol (86, X = OH) which was not purified at this stage but immediately oxidised by Jones reagent to give the unsaturated ketone (88) directly. The ketone was purified by sublimation, to furnish a colourless solid (0.3g).

A radioactive count on a sample of this material exhibited a fall off with time, and the weight of the planchet plus compound dropped from 1.21.mg. to 0.68 mgs. in the course of three hours, demonstrating the volatile nature of this compound.

The corresponding 2:4-dinitrophenylhydrazone was prepared from the ketone (45 mgs.) and after recrystallisation twice from methanol to m.p. 204-205°C proved an ideal derivative for counting. The mean activity was found to be 4.31×10^4 cpm/mM in better agreement with the value expected from calculation, (4.62×10^4 cpm/mM) than the counts on the 3-EXO tosylate.

The radioactive ketone (0.25g) was dissolved in acetone (20mls) and oxidised with acidic potassium permanganate. The acidic product was worked up as before as a yellow solid (0.07g). Careful repeated trituration with ether afforded a white solid (0.02g) of constant melting point 158-160°C previously identified as cyclohexane, 1.3 dicarboxylic acid. The relative molar activity was found to be 270 $\pm$ 10 cpm/mM.

RADIOACTIVE COUNTS

SERIES A.

3C^{14}-1-hydroxybicyclo(3.3.1)nonan-3-one

weight. (mg)	counts.	time. (Ksec.)	rate. (cpm.)	r.m.a. (cpm/mM.)
0.22	11,321	3	226.4	1.57×10^5
1.85	114,932	3	2258.6	1.91×10^5
	99,204	3	1984.1	1.65×10^5
	116,162	3	2323.2	1.93×10^5

(background : 2.0 cpm)

3C^{14} 3-EXO bicyclo(3.3.1)nonanol

0.30	9841	3	196.8	
	9565	3	191.3	
	9006	3	180.1	ca 10^5
	8725	3	174.5	see text.
	8565	3	171.3	

(background ; 2.0 cpm)

3C^{14} 3-EXO bicyclo(3.3.1)nonanyl Tosylate

2.15	13,755	3		
	13,628	3		
	13,598	3	271.96	3.69×10^4
	13,292	3	mean	mean
	13,802	3		
	13,598	3		
2.10	13,570	3		
	13,620	3		
	13,654	3	273.16	3.80×10^4
	13,702	3	mean	mean
	13,744	3		

(background ; 2.0 cpm)

C^{14}-labelled ^{3}-bicyclo(3.3.1)nonen-2-one.

1.21*	13,087	3	261.7	2.7×10^4
	11,085	3	221.7	approx.

*There was an appreciable loss of weight in the course of 3 hours (0.68mg.) (background 2.0 cpm)

C^{14}-labelled 2:4 dinitrophenylhydrazone of ^{3}-bicyclo(3.3.1) nonen-2-one.

0.25	1811	3		
	1821	3	36.24	4.38×10^4
	1794	3	mean	mean
	1786	3		
	1841	3		
0.24	1727	3	35.54	4.29×10^4
0.49	3521	3	70.4	4.30×10^4
	3499	3	69.9	4.28×10^4

(background 1.98 cpm.)

Cyclohexane-1,3-dicarboxylic acid.

3.90	410	3		
	417	3		
	403	3	8.18($\pm$ 0.065)	
	4060	30	mean	274 ± 4.
background	95	3		
	104	3		
	316	10	1.948($\pm$ 0.016)	
	316	10	mean	

Series B.

3-C^{14}-1-hydroxybicyclo(3.3.1)nonan-3-one. (82)

As before radioactive acetoacetic ester of high specific activity (1.26 x 10^{10} cpm/mM) was diluted to give 8.12g (0.062M) of approximate specific activity 3.5 x 10^{6} cpm/mM. The condensation with cyclohexenone furnished pure 3-C^{14} labelled ketol (82, 3g) with a somewhat lower incorporation of radioactive label. The relative molar activity was found to be 1.51 x 10^{5} cpm/mM.

3-C^{14}-3-EXO bicyclo(3.3.1)nonanol. (84)

The radioactive ketol (3g) was diluted with unlabelled material (2g) and converted to the bromo-ketone in high yield (6g). Lithium-liquid ammonia reduction as before produced 3C^{14}-3-EXO alcohol, which was purified by chromatography, then recrystallised from pentane, in 40% overall yield (1.722g, 11.5mM).

3-C^{14}-3-EXO bicyclo(3.3.1)nonyl-p-toluenesulphonate. (85)

The radioactive alcohol (1.722g) was converted smoothly to its tosylate ester, which after two recrystallisations furnished colourless plates (2.276g, 7.74mM) of m.p. 58-59°C.

The relative molar activity was measured as 7.0 x 10^{4} cpm/mM and, as in the previous series, this was lower than might be expected from the dilutions involved. (9 x 10^{4} cpm/mM).

Acetolysis of 3C^{14}-3 EXO bicyclo(3.3.1)nonyl-p-toluenesulphonate (85)

The radioactive tosylate (2.276g, 7.74mM) and fused sodium acetate (0.70g, 8.51mM) were dissolved in anhydrous acetic acid (77 mls) warmed to 80° and maintained at this temperature for 96 hours.

The reaction was cooled and worked up as described before to afford an oil (approx. 1.0g). The radioactive solvolysis products were compared with the products of earlier experiments by GLC and were found to be typical.

Chromatographic separation furnished the radioactive olefin (0.8g) free from the mixture of epimeric acetates. The hydrocarbon was divided into two portions and one was set aside for further study.

Degradation of C^{14}-labelled 2-bicyclo(3.3.1)nonene. (86)

The radioactive olefin (0.40g) obtained from acetolysis of 3C^{14} 3 EXO tosylate was subjected to selenium dioxide oxidation in aqueous dioxane as before, to produce the allylic alcohol (87, X = OH), which was purified by chromatography.

The alcohol was then oxidised with Jones solution at 0°C to give the unsaturated ketone (88) as a colourless solid (0.135g). The dinitrophenylhydrazone derivative was prepared, m.p. 203-204°C, and the relative molar activity was found to be 9.93 x 10^4 cpm/mM.

Oxidation of the radioactive ketone (0.125g) with acidic potassium permanganate solution produced a semi-solid acidic product (0.04g). Trituration with ether produced 89, as a colourless solid of mp. 158-162°C. Recrystallisation from ether-pentane (10:1) to constant m.p. 160-164°C gave cyclohexane, 1,3 diacid of relative molar activity 3.76×10^3 ($\pm$ 0.06) and 3.35×10^3 ($\pm$ 0.08) cpm/mM from two successive recrystallisations. The C^{14} incorporation was calculated as 3.58%.

RADIOACTIVE COUNTS

SERIES B.

$3C^{14}$-1-hydroxybicyclo(3.3.1)nonan-3-one.

weight. (mg)	counts.	time. (Ksec)	rate. (cpm.)	r.m.a. (cpm/mM.)
0.45	22069	3	441.4	
	21949	3	438.9	1.50×10^5
	22216	3	444.3	mean
0.44	218517	3	437.0	1.52×10^5

(background : 2.00 cpm)

$3C^{14}$-3 EXO bicyclo(3.3.1)nonanyl Tosylate.

3.00	36012	3	720.2	7.04×10^4
	359664	30	719.3	mean
1.27	15371	3	307.4	7.05×10^4

(background : 2.53 cpm)

C^{14}-labelled 2:4-Dinitrophenylhydrazone of 3-bicyclo(3.3.1)nonan-2-one.

1.10	17600	3		
	17553	3	350.3	9.96×10^4
	173939	30	mean	mean

(background : 2.70 cpm)

C^{14}-labelled Cyclohexane-1,3-dicarboxylic acid.

1.02	1235	3	25.076	3.76×10^3
	1254	3		
	12724	30	(±0.216)	(±0.06)
0.92	1035	3		
	989	3		
	10547	30	20.70	3.35×10^3
	10621	30	(±0.33)	(±0.08)
background	135	3	2.75	
	140	3	(±0.05)	

Epimeric 7-Exo-methyl-3-bicyclo(3.3.1)nonanols.(31, 42).

Samples of the 7-exo-methyl 3 exo and 3 endo alcohols, (0.25g and 0.025g respectively) were kindly supplied by Dr. S. Graham. The epimeric alcohols were not separable under the GLC conditions available, however the corresponding acetates (see below) were readily resolved. By acetylation procedures described above the epimeric purity of the sample of 3-exo alcohol (31) was shown to be greater than 96%, whereas that of the 3-endo alcohol (42) was less than 90%.

7-Exo-methyl-3-exo-bicyclo(3.3.1)nonanol. (31)

The sample supplied had ν_{max} (high resolution, CCl_4) 3630a, 1461, 1456, 1444, 1376, 1365, 1320, 1090, 1026, 950 and 917 cm^{-1}. NMR (100 Mc). 9-line multiplet centred @ 5.80 (1H, X part of an A_2B_2X system; J_{AX} = 11.0, J_{BX} = 6.0 c/s.), sharp singlet @ 6.60 (1H, hydroxyl) complex methylene and methine resonance @ 8.00-9.00 (13 H) and a sharp doublet centred @ 9.18 (CH_3 group, J = 4 c/s.).

Acetate (121)

A sample (5 mg) of the 3-exo alcohol (31) was acetylated as before and GLC analysis indicated the presence of 7-exo-methyl-3-exo-bicyclo(3,3,1)nonanyl acetate (R.I. 1370 96%) and its 3-endo epimer (R.I. 1380 4% or less).

Toluene-p-sulphonate.(98)

The tosylate ester was prepared in the usual manner from 7-exo-methyl-3-exo-bicyclo(3,3,1)nonanol (0.047g, 0.30mM) and toluene-p-sulphonyl chloride (0.061g, 0.32mM) to furnish crystals of 7-exo-methyl-3-exo-bicyclo(3,3,1) nonanyl tosylate (98, 0.065g) of m.p. 68-69°C,(after two recrystallisations from pentane), ν_{max} (mull) 3050, 1600, 1190, 945, 880, 795 and 680 cm^{-1}. free from hydroxylic absorption. The tosylate wa thermally unstable, decomposing above the melting point in the solid state.

7-Exo-methyl-3-endo-bicyclo(3.3.1)nonanol. (42)

The sample supplied had ν_{max} (mull) 3300, 1465, 1455, 1380, 1340, 1265, 1095, 1060, 950 and 820 cm^{-1}. NMR(100 Mc). Complex asymmetric signal @ 6.20 (carbinyl proton base line separation, ca 34 c/s). Complex methylene and methine resonance @ 7.80-9.00 with hydroxyl proton superimposed, and a sharp doublet centred @ 9.18 (CH_3 group, J = 4 c/s.).

Acetate (122)

A sample (3 mg.) of the 3-endo alcohol (42) was acetylated as before and GLC analysis indicated the presence of 7-exo-methyl-3-endo-bicyclo(3,3,1)nonanyl acetate (R.I. 1380, 90%) and its 3-exo epimer (R.I. 1370 10%).

Toluene-p-sulphonate (97)

The tosylate ester was prepared in the usual manner from the 3-endo alcohol (16.0 mg, 0.10mM) and toluene-p-sulphonyl chloride (25.0 mg, 0.11mM) but was obtained as an oil contaminated with starting alcohol ν_{max} (film) 3300, 3050, 1600, 1195, 1190, 1095, 1060, 950, 880, 830, 795, 740, 720 and 680 cm^{-1}. 7-exo-methyl-3-endo-bicyclo(3,3,1)nonanyl toluene-p-sulphonate (97) was not obtained in a pure state, nor did the sample crystallise and was comparable with the nor-methyl compound (53).

Acetolysis of 7-Exo-methyl-3-exo-bicyclo(3.3.1)nonanyl Toluene-p-sulphonate. (98).

The tosylate ester (0.03g, 0.1mM) and fused sodium acetate (0.009g, 0.11mM) were dissolved in anhydrous acetic acid (10 ml.) and the solution maintained at room temperature for 24 hours (ca. 12 half-lives). The solvolysis products were isolated as before and examined by GLC. The hydrocarbons produced were shown to be a mixture of ^{2}-7-exo-methylbicyclo(3,3,1)nonene (22) and ^{2}-3-methylbicyclo(3,3,1) nonene (25) in the ratio of 43:55 respectively, by comparison with authentic samples of these compounds kindly supplied by Dr. S. Graham. The acetates produced (estimated as less than 2% of the total products) were shown to have the same retention times as 7-exo-methyl-3-exo-bicyclo(3,3,1)nonanyl acetate (121) and its 3-endo epimer (122) and were formed in the ratio of 3:2 respectively.

Acetolysis of 7-Exo-methyl-3-endo-bicyclo(3.3.1)nonanyl Toluene-p-sulphonate (98).

Only preliminary results have been obtained as yet. The tosylate ester (ca 0.03g, 0.1mM) contaminated with 3-endo alcohol (42) ignored in the product analysis, and sodium acetate (0.009g, 0.11mM) were dissolved in anhydrous acetic acid (10 mls) and the solution maintained at room temperature for 24 hours. The solvolysis products were isolated as before, examined by GLC and shown to be a mixture of the

same olefinic products as above, 7-exo-methyl-^{2}-ene (22) and 3-methyl-^{2}-ene (25) in the ratio of 1:5 respectively. The acetates produced (estimated as less than 3% of the total products) were shown to have the same retention times as the 3-exo acetate 121 and the 3-endo acetate 122, and were produced in approximately equal amounts (ca 1.5%).

7-Exo-methylbicyclo(3.3.1)nonan-3-one (103).

A. The 3-exo alcohol (31, 0.025g) was oxidised by the method of Jones [58] to afford the corresponding ketone, 7-exo-methyl-bicyclo(3,3,1)nonan-3-one in good yield. After recrystallisation from pentane colourless crystals were obtained, of m.p. 49-51°C, ν_{max} (high resolution, CCl_4) 1715, 1702, 1458a, 1438, 1411, 1405, 1378, 1352, 1342, 1335, 1225, 1121a, 1116, 1088, 958, and 872 cm^{-1}. NMR (100 Mc), sharp singlet @ 7.57 (6H), complex methylene and methine resonance @ 8.20-8.80 (7H) and a sharp doublet centred @ 9.14 (CH_3 group, J = 4 c/s.).

B. Anti-7-exomethylenebicyclo(3,3,1)nonan-3-ol* (101, 0.01g) was added to concentrated sulphuric acid (75%, 3ml.) and the mixture heated to approximately 60°C for 15 minutes. The colourless solution was poured onto ice (15g), neutralised

* See section II

with solid sodium bicarbonate, then extracted with pentane (3 x 10 ml.). The combined organic phase was washed with saturated sodium bicarbonate solution, then brine, dried ($MgSO_4$) and the solvent removed. The crystalline product (9 mg.) ν_{max} (mull) 1710, 1470, 1415, 1380, 1355, 1230, 1130 and 1100 cm^{-1}. was homogeneous to TLC and GLC, and was identical with 7-exo-methylbicyclo(3,3,1)nonan-3-one (103). The mass spectrum (GCMS) was also shown to be identical with that obtain d for the material produced above. Mass spectral parent ion 152 (35%), p+1 153 (4%). relative to base peak 95 (100%).

7-Endo-deutero-7-exo-methylbicyclo(3.3.1)nonan-3-one. (105)

Anti-3-endo-deutero-7-exomethylenebicyclo(3,3,1)nonan-3-ol * (104, 0.120g) was treated with 75% sulphuric acid as described above, and afforded a crystalline ketonic product in excellent yield (0.110g) which was purified by sublimation to furnish prisms of m.p. 55.5-56.5°C, ν_{max} (high resolution, CCl_4) 2950, 2014, 2869, 2851, 2841, 2144, 1722, 1708, 1458, 1454, 1438, 1412, 1405, 1376, 1360, 1340, 1325, 1242, 1222, 1099 and 932 cm^{-1}. NMR (100 Mc), singlet @ 7.58 (6H), four groups of peaks @ 8.20-8.90 (6H) and a sharp singlet @ 9.16 (CH_3 group) compatible with the specifically monodeuterated title compound. Mass spectral analysis (GCMS) indicated a high deuterium content, greater than 98%: parent ion 153 (36.5%), p+1 ion (5%), p-1 ion (1.4%).

7-Endo-deutero-7-exo-methyl-3-exo-bicyclo(3.3.1)nonanol (106).

Lithium (0.5g) was dissolved in liquid ammonia (75 ml) in a flask fitted with an efficient acetone - $CO_{2(s)}$ condenser, and a dropping funnel by means of which a solution of mono-deutero-7-exo-methyl-3-ketone (105, 0.090g) and tertiary butanol (0.30g) in ether (10 ml.) was added slowly. The solution was stirred for 2 hours.

Ether-methanol (1:1) was added slowly to the reaction to destroy excess lithium. When the blue colour was discharged, the liquid ammonia was allowed to evaporate as pentane (10 ml) and saturated ammonium sulphate solution (10 ml) were added.

The reaction was allowed to warm up to room temperature, then dilute hydrochloric acid (6N, 15 ml) was slowly added and the resulting two phase mixture separated. The aqueous phase was further extracted with pentane (3 x 30 ml) and the combined organic phase washed with dilute hydrochloric acid (3N, 30 ml), saturated sodium bicarbonate solution (30 ml), then brine (30 ml), dried ($NaSO_4$) and the solvent removed under reduced pressure, to yield 7-endo-deutero-7-exo-methyl-3-exo-bicyclo(3,3,1)nonanol (106).

The crude product (0.080g) a pale yellow solid, $_{OH}$ 3300 and $_{CD}$ 2170 cm^{-1} was shown to consist of 3 compounds by TLC; one major product (rf 0.3 stained purple) and traces of 2 less polar compounds (rf 0.5 and 0.7). A small portion was

acetylated and GLC analysis showed the product to be almost pure equatorial alcohol (94%).

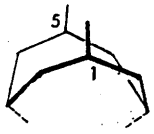
Recrystallisation from pentane followed by sublimation (at 70°C/3 mm. pressure) afforded colourless crystals (0.019g) of m.p. 61-63°C, homogeneous to TLC and GLC. The mother liquors were evaporated then chromatographed to obtain further product (0.027g). ν_{max} (CCl_4, high resolution) 3630(a), 2946, 2919, 2867, 2850, 2841, 1463, 1453, 1442, 1375, 1366, 1301, 1064, 1033, 960 and 918 cm^{-1}.

NMR (100Mc): 9-line multiplet centred @ 5.80 (1H, X part of an A_2B_2X system, J_{AX} = 11c/s, J_{BX} = 6 c/s), six groups of peaks @ 7.95 - 8.95 (12H) with a sharp singlet superimposed @ 8.76 (1H, by hydroxylic) and a sharp singlet @ 9.18 (3H).

7-Endo-deutero-7-exo-methyl-3-exo-bicyclo(3.3.1)nonyl Toluene-p-sulphonate. (99)

Treatment of the monodeuterated 7-exo-methyl-3-exo alcohol (106) with toluene-p-sulphonyl chloride in the usual manner supplied the tosylate ester (99) which recrystallised from pentane as colourless plates, m.p. 62.5 - 63°C; ν_{max} (mull) 2180, 1180, 940, 870, 830, 785 and 675 cm^{-1}.

The tosylate ester was subjected to acetolysis at 25.0°C and the rate of reaction measured, see Appendix A.



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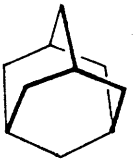

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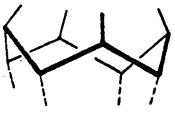

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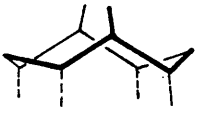

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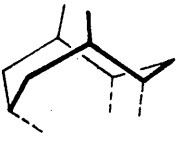

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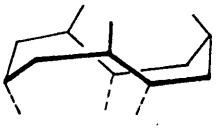

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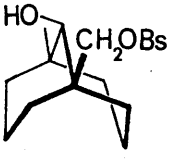

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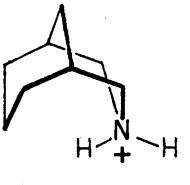

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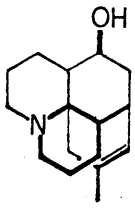

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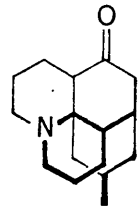

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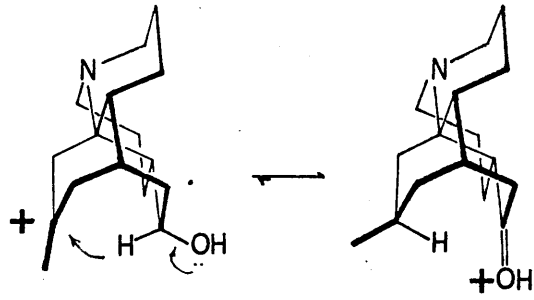

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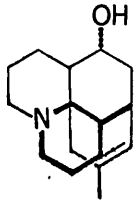

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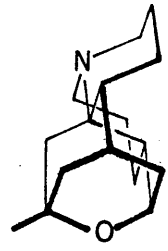

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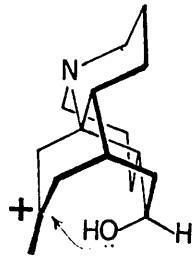

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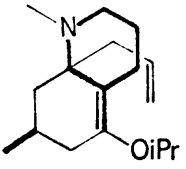

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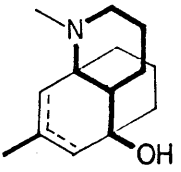

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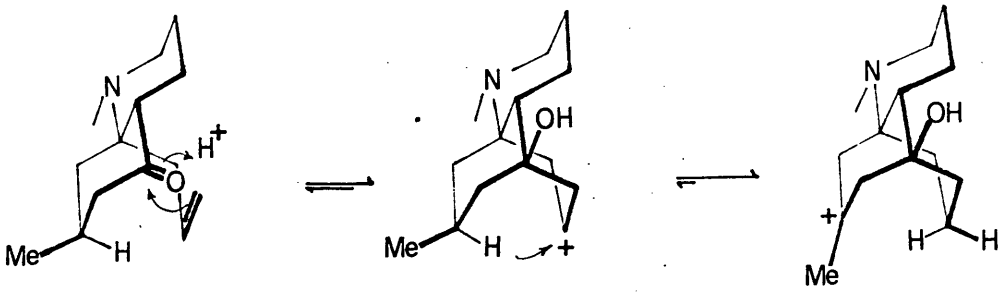

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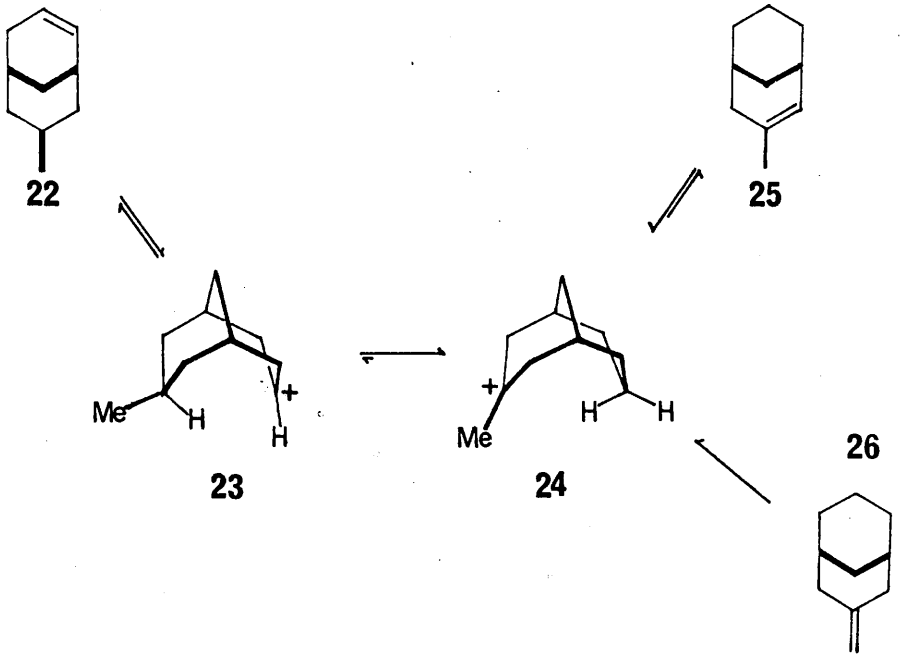

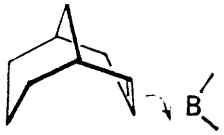

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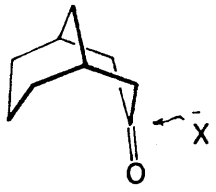

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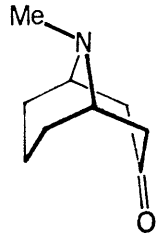

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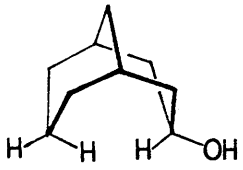

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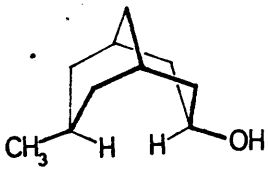

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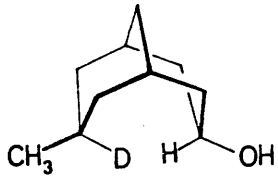

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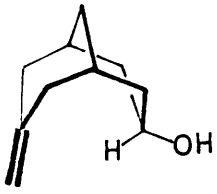

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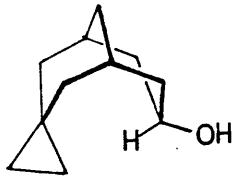

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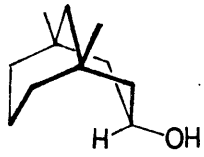

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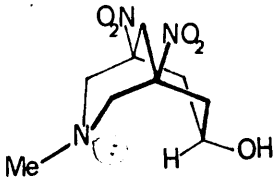

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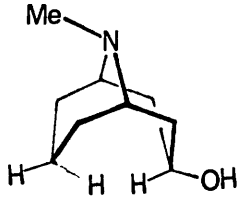

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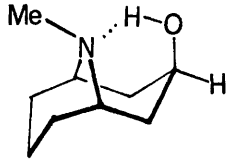

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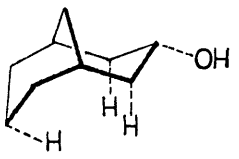

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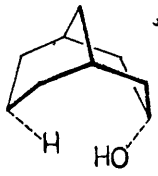

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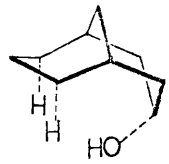

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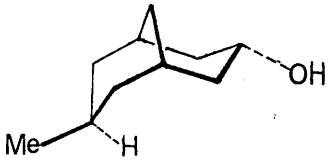

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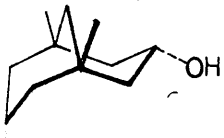

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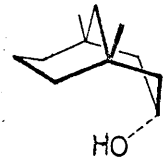

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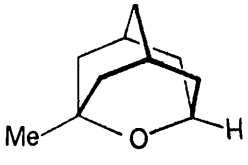

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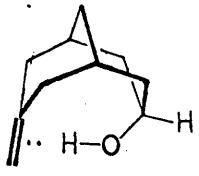

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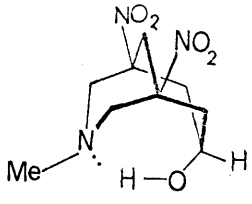

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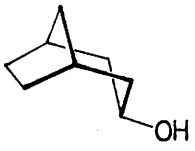

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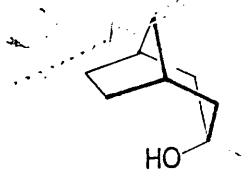

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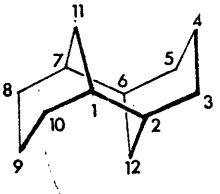

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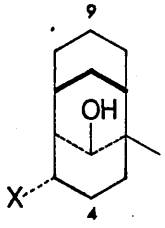

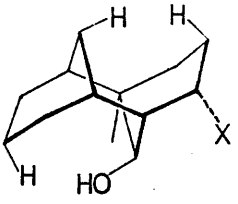

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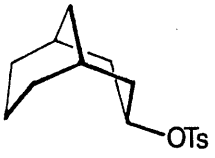

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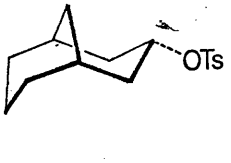

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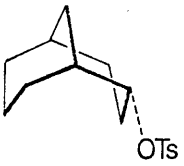

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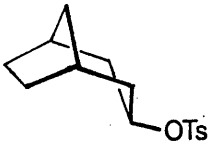

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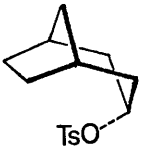

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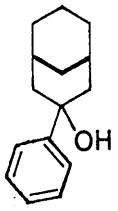

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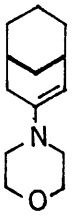

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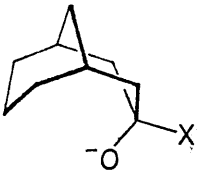

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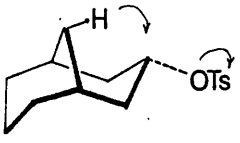

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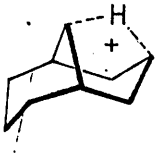

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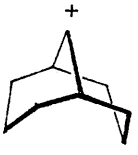

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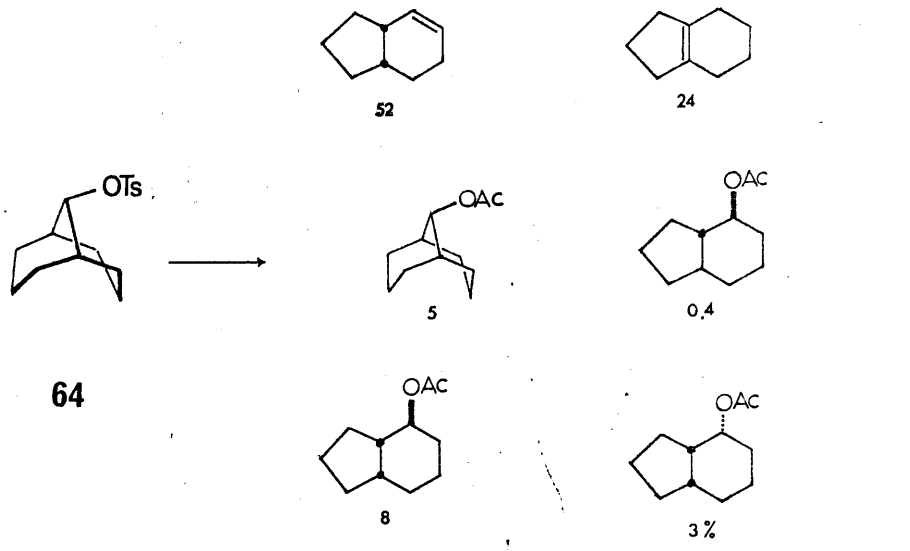

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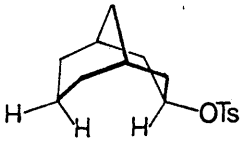

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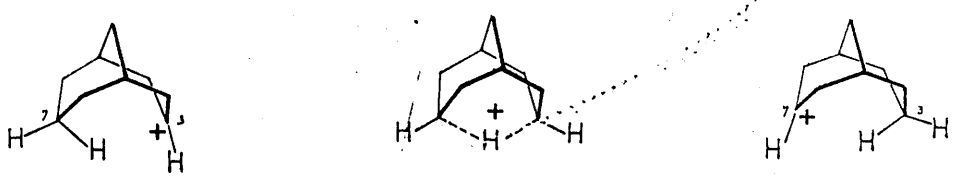

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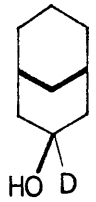

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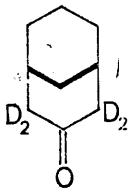

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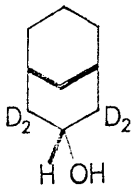

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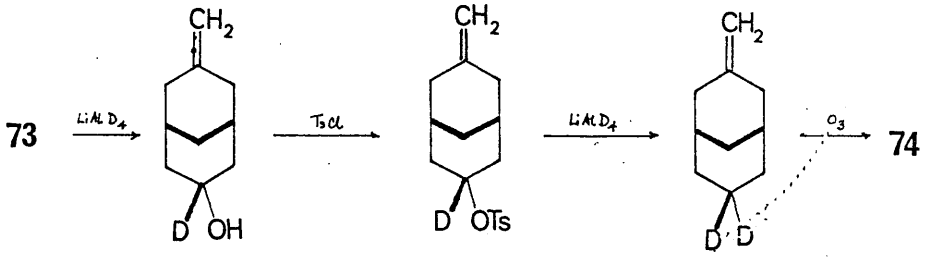

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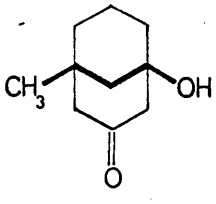

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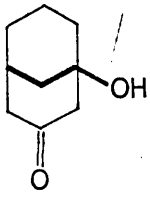

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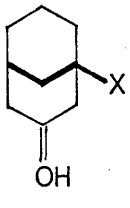

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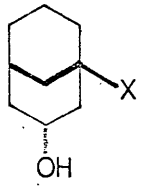

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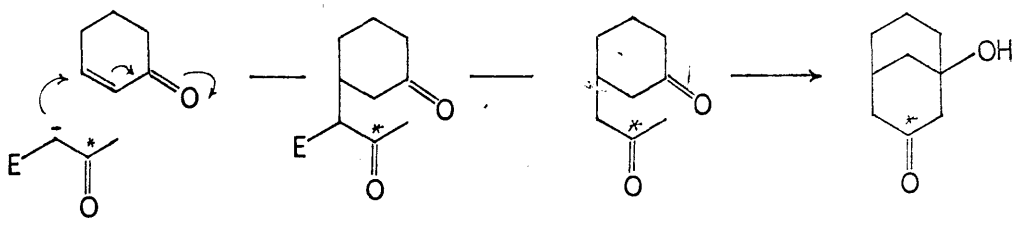

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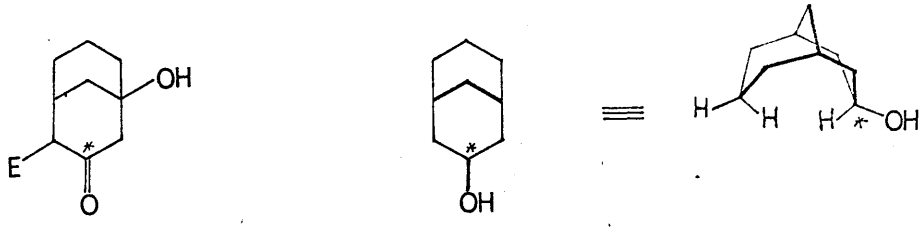

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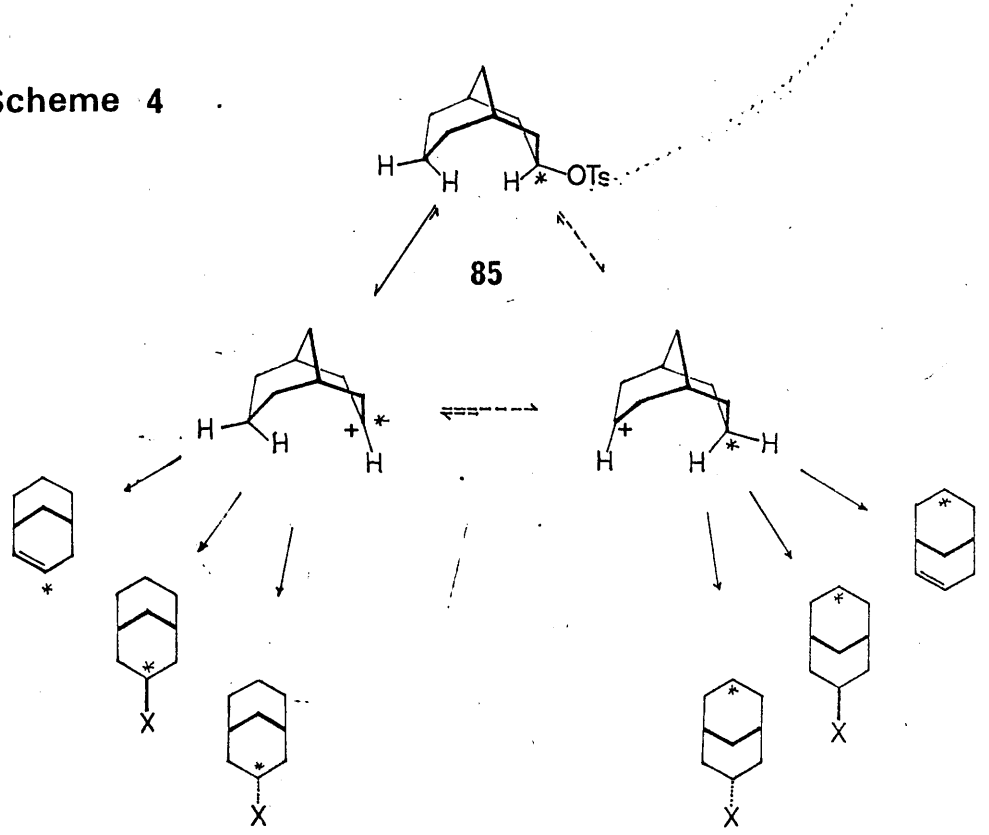

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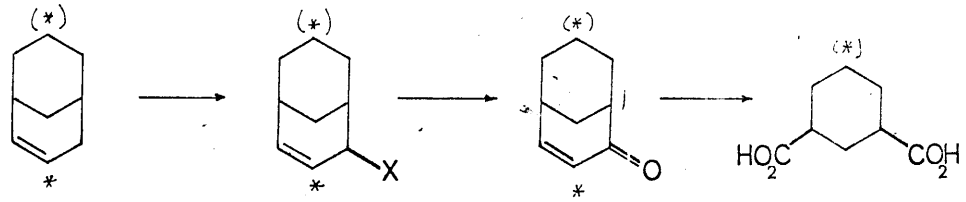

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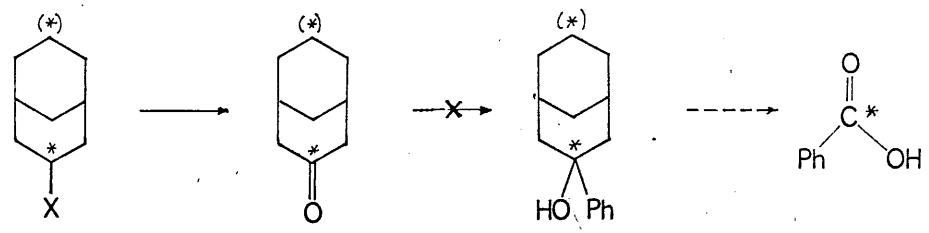

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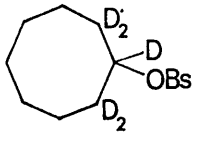

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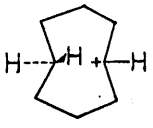

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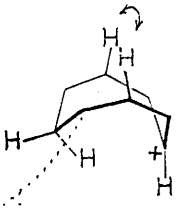
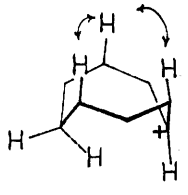


93



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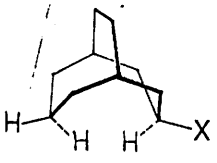

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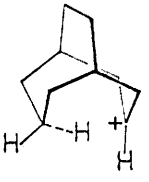

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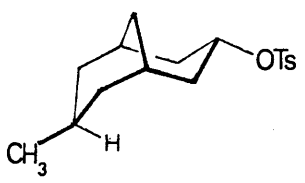

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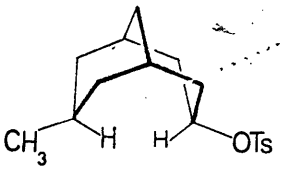

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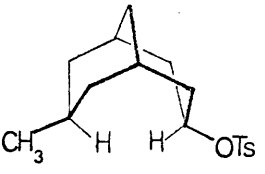

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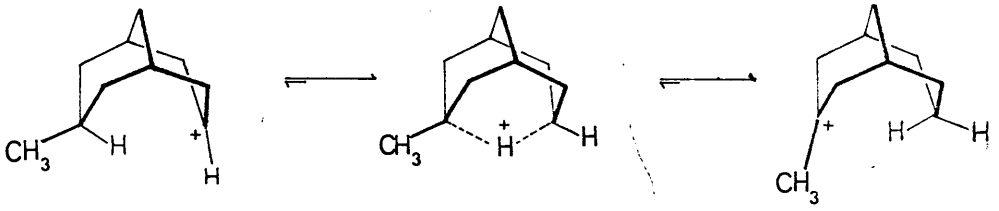

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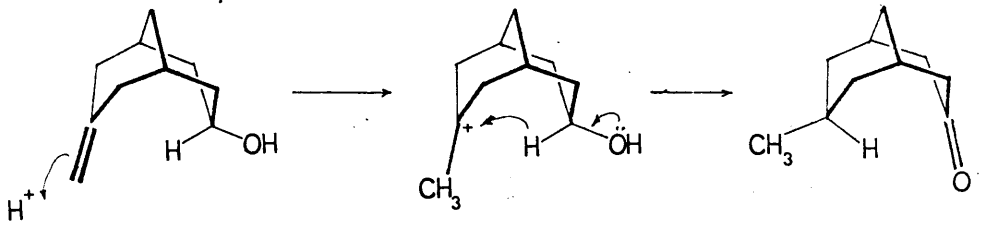
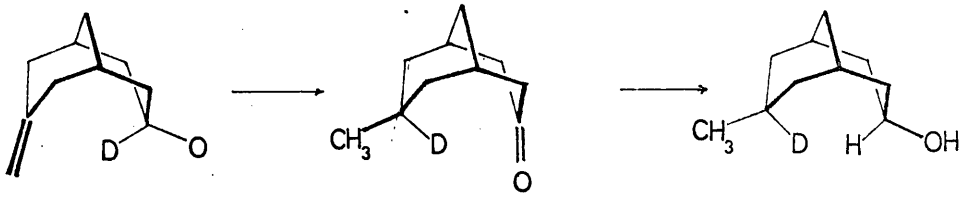
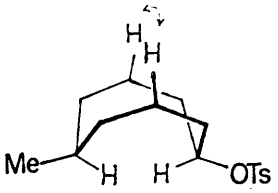


101 102 103



104 105 106



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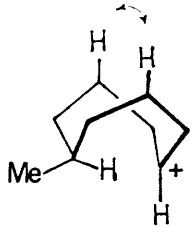

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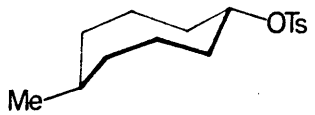

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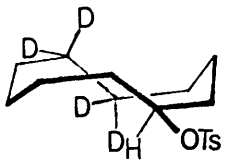

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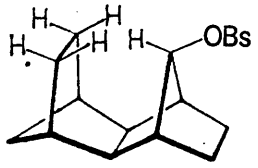

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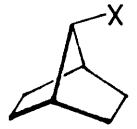

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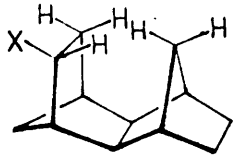

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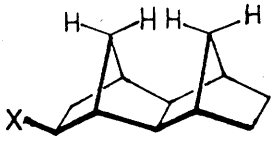

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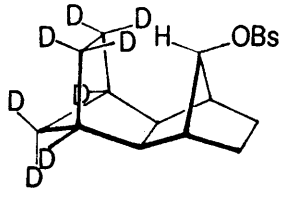

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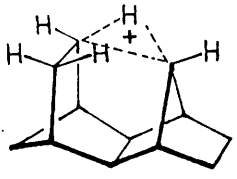

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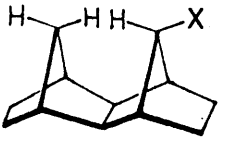

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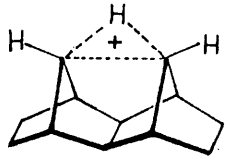

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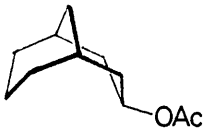

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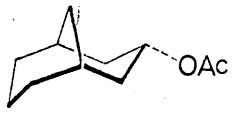

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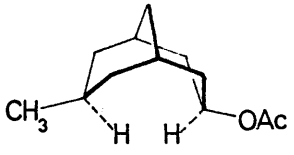

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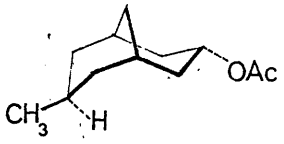

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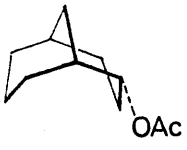

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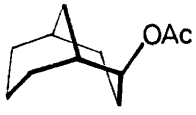

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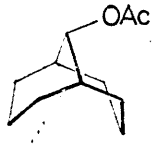

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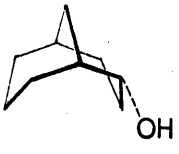

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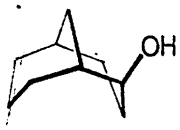

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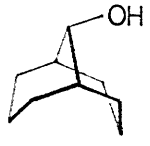
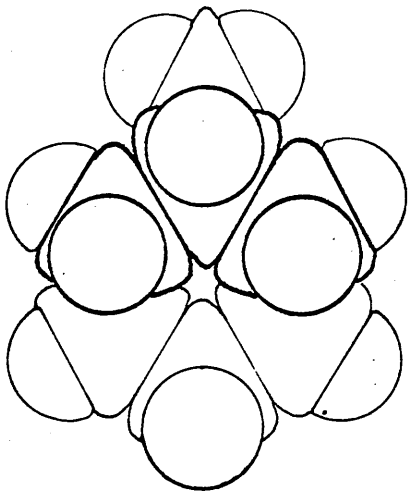


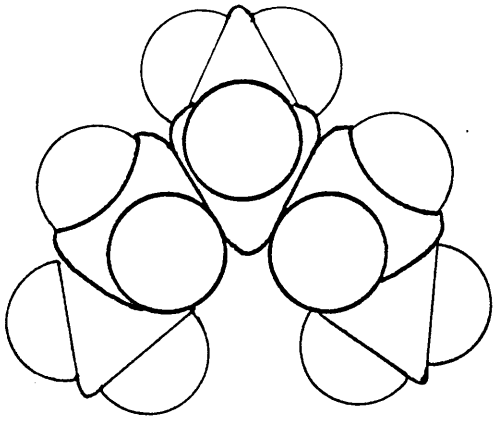
128

FIG. 1

a.



b.



c.

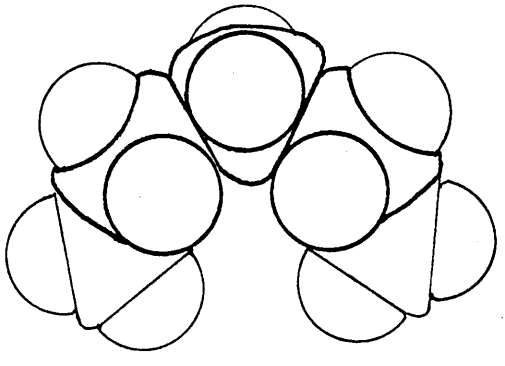
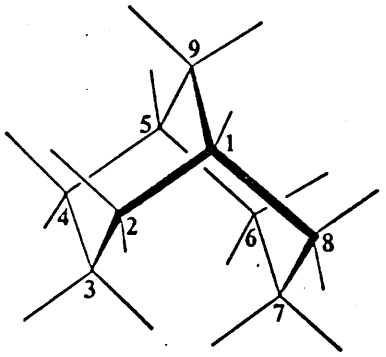
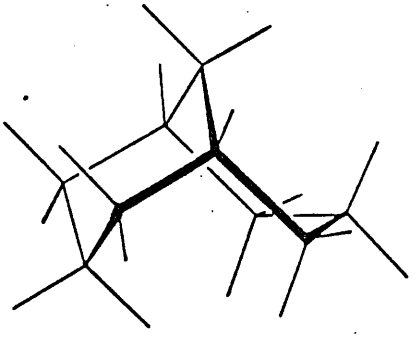


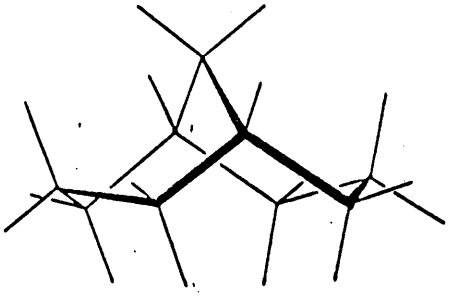
FIG. 2



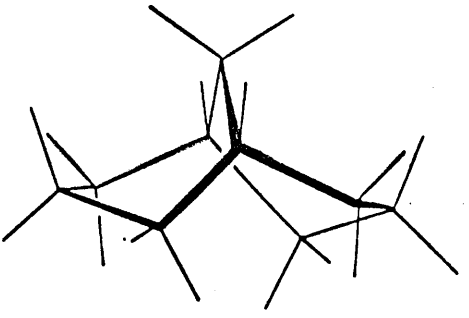
a. Twin-Chair



b. Boat-Chair



c. Twin-Boat



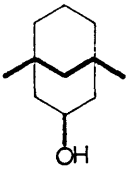
d. Twin-Twist-Boat

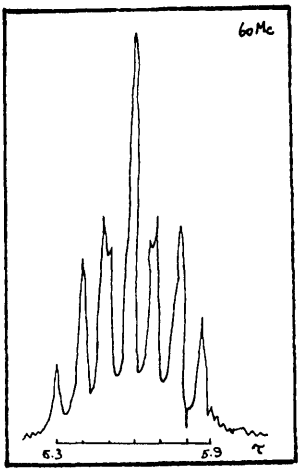
FIG. 3

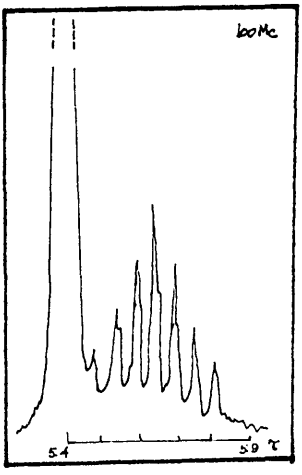
30

33

35







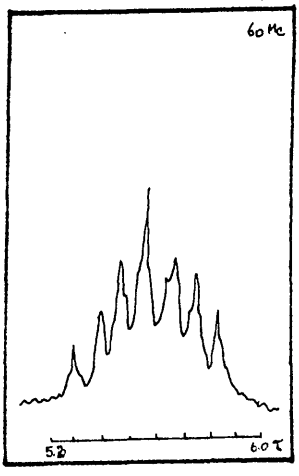
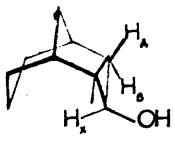
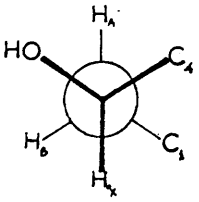
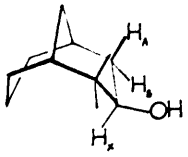
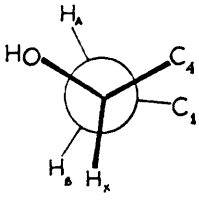
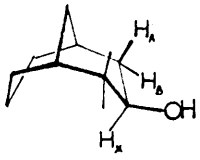
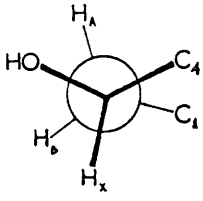


FIG. 4

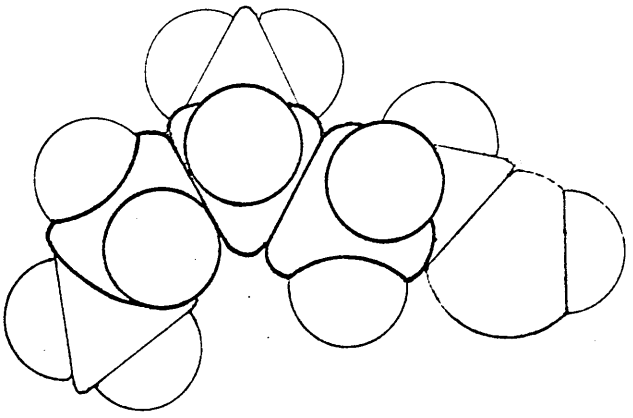
Conformation	Projection C_3C_2	ϕ	*J (c/s)
		AX 180° BX 60° AB 120° C_1C_4 60°	16.0 2.5
a.			
		AX 152° BX 32° AB 120° C_1C_4 32°	11.0 7.2
b.			
		AX 152° BX 40° AB 112° C_1C_4 41°	11.0 6.0
c.			

* $J = 10\cos^2\phi$ $\quad 0 \leqslant \phi \leqslant 90$

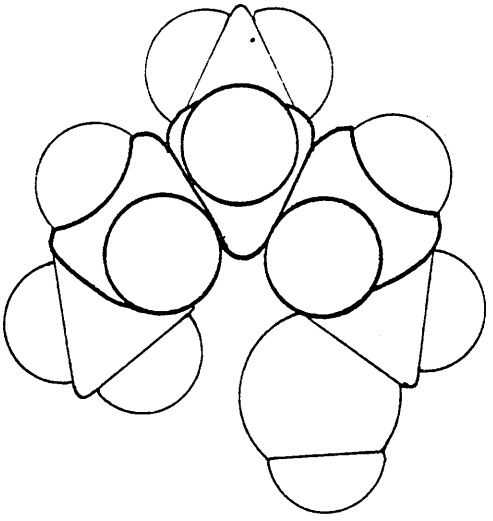
$J = 16\cos^2\phi$ $\quad 90 \leqslant \phi \leqslant 180$

FIG. 5

a.



b.



c.

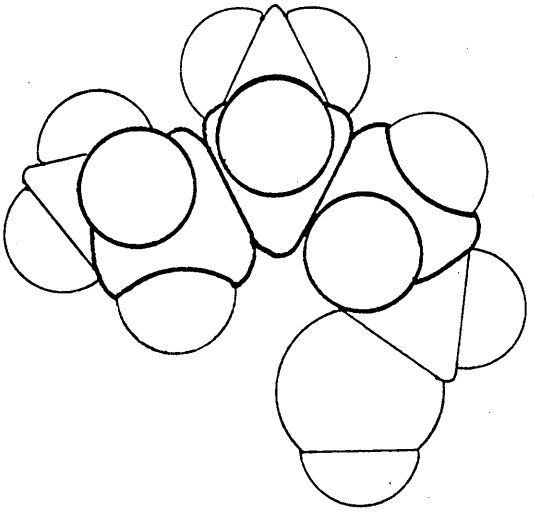


FIG. 6

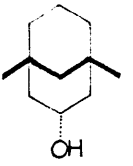
39

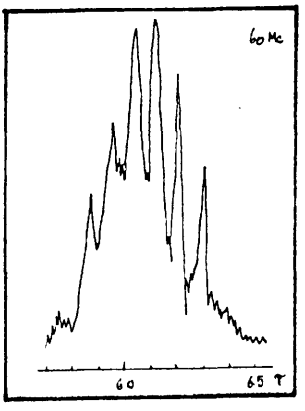

OH

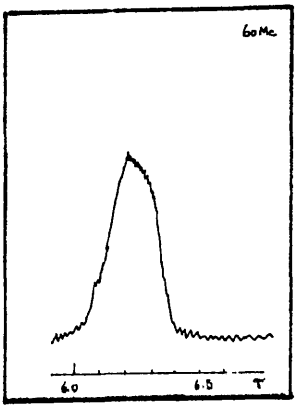
46

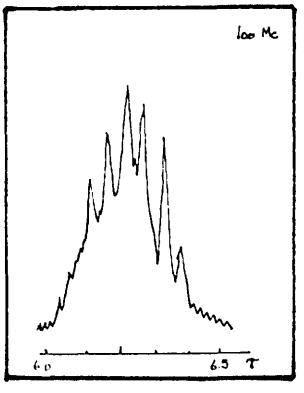

CH2
OH

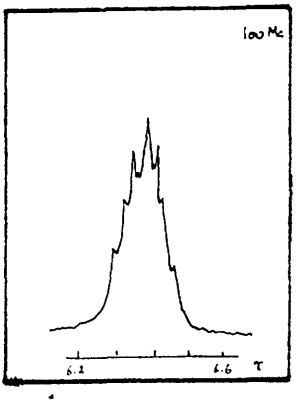
43


OH


60 Mc
6.0
6.5 τ


60 Mc
6.0
6.5 τ


100 Mc
6.0
6.5 τ


100 Mc
6.2
6.6 τ

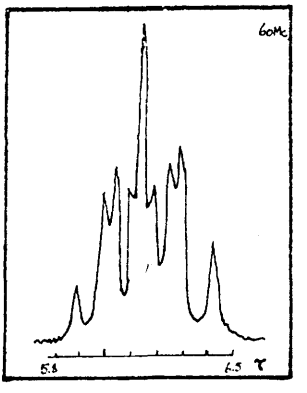

60Mc
5.8
6.5 τ

FIG. 7

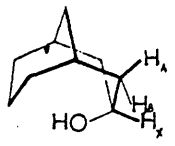
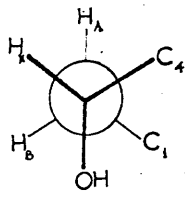
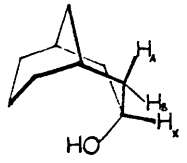
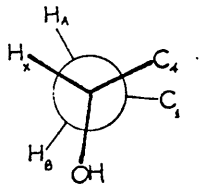
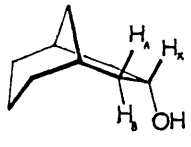
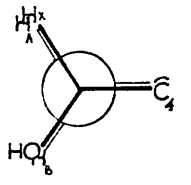
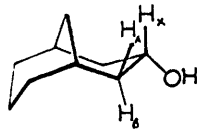
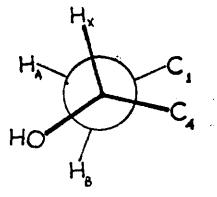
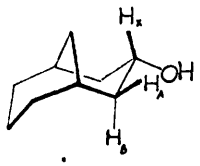
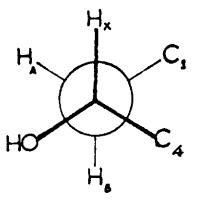
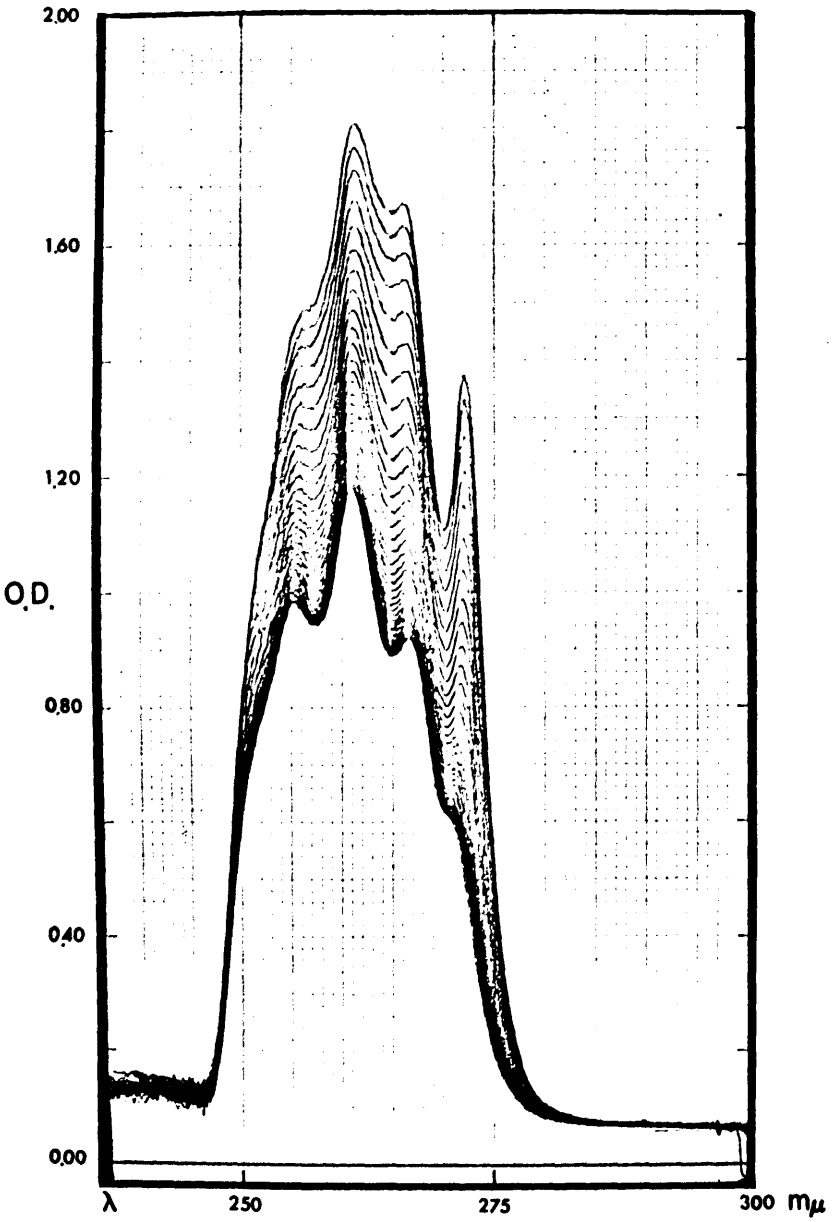
	Conformation	Projection C_3 C_2	$J_{AX} + J_{BX}$
a.			5
b.			5 - 14
c.			14
d.			14 - 18.5
e.			18.5

FIG. 8



UV SPECTRUM OF **52** AT 50°C, ACETOLYSIS.

APPENDIX A.

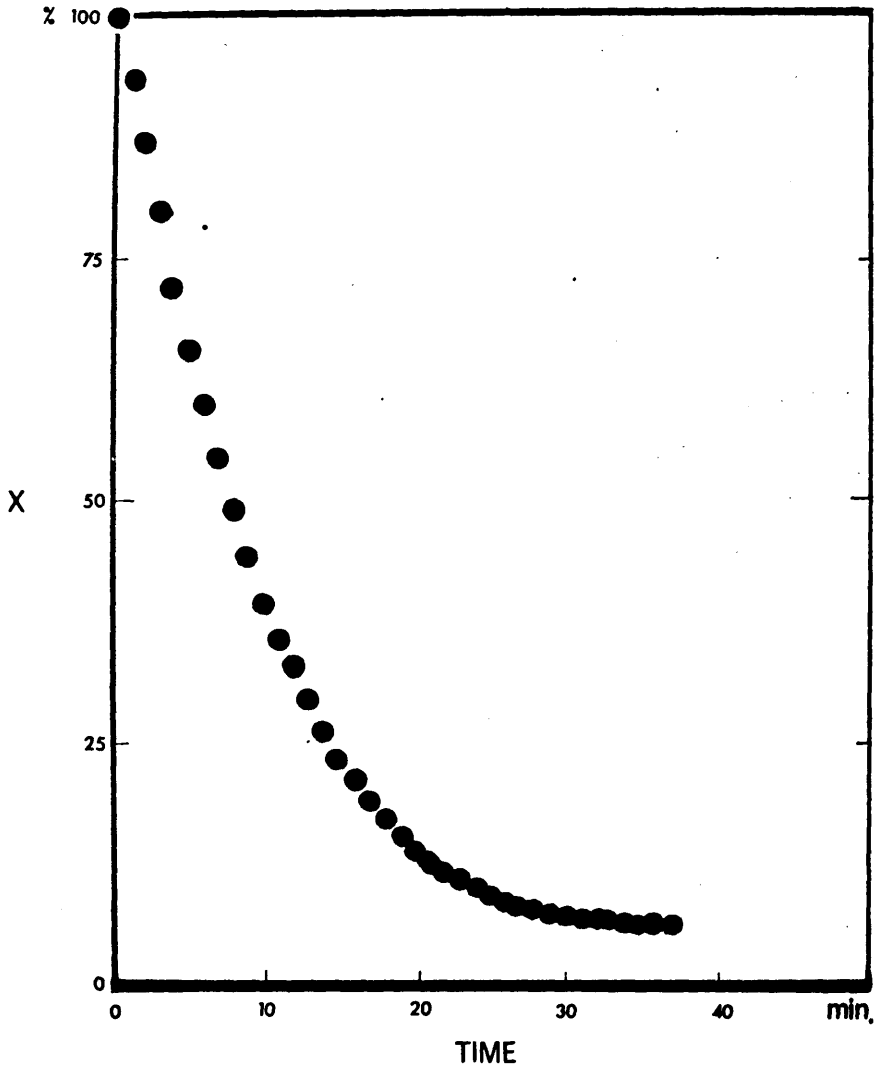
RATE MEASUREMENTS.

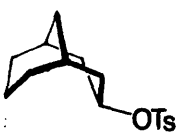
The paucity of several of the toluene-p-sulphonate esters prompted the use of the spectrometric method of measuring the reaction kinetics described by Swain and Morgan [134]. The method is dependent upon the difference in absorption of the tosylate ester and the tosylate anion; at 261 m , methyl tosylate (in water) has an extinction coefficient of 671 whereas that of tosylate anion is 344.

The rate of reaction can be followed by measuring the decrease in optical density with time. The results obtained for the first order rate constant of the hydrolysis of methyl tosylate by this method have been shown to be in excellent agreement with data obtained by conductiometric methods [134].

The application of the same method to solvolytic reactions in buffered acetic acid was found to give consistent results, and a modification of the sampling method used by the authors enabled rate measurements to be carried out on extremely small quantities of material. The original method involved taking aliquots from the reaction solution in a thermostated bath, at appropriate intervals and measuring the UV absorption. With the equipment available it was possible to thermostat the UV cells inside the spectrometer, and this allowed the continuous monitoring

FIG. 9





at 50°C.

of the solvolysis reaction.

ACETOLYSIS PROCEDURE. A solution of fused sodium acetate in anhydrous acetic acid made up in a 100 ml graduated flask was allowed to equilibrate in the constant temperature bath which thermostated the cell units in the UV spectrometer. A sample of the appropriate tosylate (2.0-2.5 mg) was placed in a 1 cm. silica UV cell. The reference cell was filled with the buffered acetic acid solution, stoppered and placed in the reference beam. The scan-mode was then selected (vide infra); acetolyses were usually followed individually and the region 240 - 300 m was scanned automatically at a preselected interval (figure 8). When simultaneous reactions were being measured the constant-wavelength scan was selected, locked at 262 m and the appropriate cells moved into position automatically. The sample cell was then filled with the buffered acetic acid solution, stoppered, shaken thoroughly and inserted in position. Automatic recording was then started and continued for a period of 10 half-lives, although with the less reactive compounds, the reaction was followed to approximately 70% completion and an infinity reading obtained after the appropriate interval.

KINETICS. The decreasing optical density at 262 m was noted with time. The percentage unreacted tosylate (X) was calculated at each reading, and was found to decrease in an exponential manner (figure 9). The initial concentration

of tosylate ester could be calculated from the infinity reading. The half-life and 1st order rate constant (k_1) of the reaction were obtained graphically from a plot of the logarithm of the percentage unreacted tosylate ($\log_{10} X$) versus time. Thermodynamic quantities were calculated by means of the following equations: [35]

$$H^{\ddagger} = 4.575 \frac{T_2 . T_1}{(T_2 - T_1)} . \log_{10} \frac{k_2 . T_1}{k_1 . T_2}$$

$$S^{\ddagger} = \frac{H}{T} + 4.575 (\log_{10} \frac{k}{T} - 13.876)$$

In the above equations,

$H^{\ddagger}$ = enthalpy of activation

$S^{\ddagger}$ = entropy of activation

T = absolute temperature

k = reaction rate constant ($hr.^{-1}$)

In the case of exo-bicyclo(3,3,1)nonan-3-yl tosylate data was available at more than two temperatures, and $H^{\ddagger}$ was calculated from the gradient of the plot of $\log_{10} k/T$ against $1/T$. [41]

RESULTS. The results obtained are summarised in the following pages. The compounds examined all displayed first-order kinetics in acetolysis. Due to the reactivity of the compounds under investigation it was difficult to measure the rate of solvolysis at temperatures above 50°C. The data obtained for the 3 exo tosylate at 70° and 80°C does not reflect deviation from first-order kinetics, but rather acceleration of the reaction rate as the temperature of the cell contents rises to the reaction temperature. If the UV spectrum were measured after equilibration, the reaction was at least 70% complete. By measuring the process as equilibration occurred the results shown were obtained and if the tangent to the resulting curves is taken as the limiting rate at the given temperature, the derived kinetic data is reproducable.

At lower temperatures, more precise thermostating was possible since the reaction rate was appreciably slower and the above effect is absent at 25°C. This method of rate measurement was ideal for the compounds under investigation since the reaction periods were relatively short and adequate temperature control could be maintained throughout. The method was checked by measuring the rate constant for the acetolysis of cyclohexyl tosylate, and was found to give results in good agreement with published data.

Solvent.

The anhydrous acetic acid used in all the solvolysis experiments was prepared from glacial acetic acid ("Analar" reagent) according to the method of Winstein.[xxx] The fraction of b.p. 118-120°C was collected and used.

Toluene-p-sulphonates.

The preparation of the various tosylates have been described in the previous experimental section, as have the products of acetolysis.

Sodium Toluene-p-sulphonate.

Toluene-p-sulphonic acid monohydrate (31.2 mg 1.64 mM) was dissolved in buffered acetic acid (50 ml, 5.07×10^{-3} M in NaOAc) to give a solution 3.28×10^{-3} M in tosylate anion; λ_{max} 262 m , ε 349.

Spectrometer.

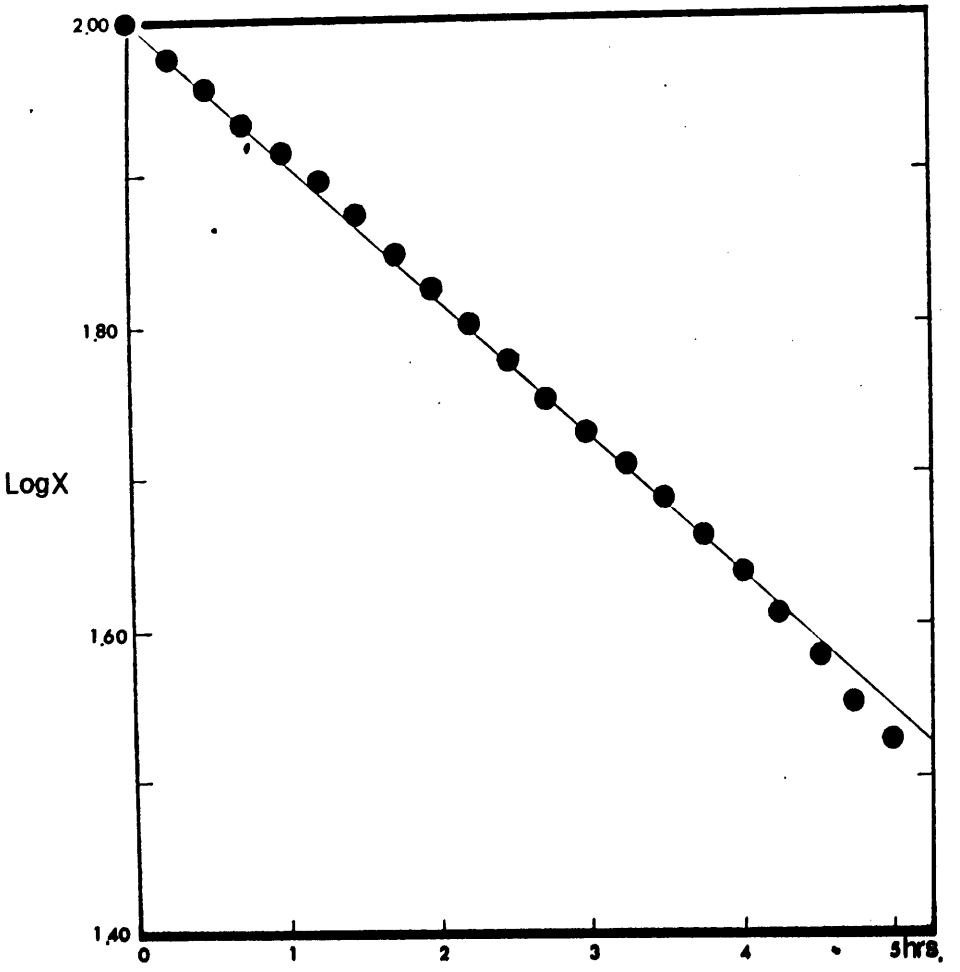
The instrument used was a Unicam S.P.800 ultra-violet spectrometer equipped with a special cell holder, linked to an automatic selection mechanism, and capable of thermostating 4 pairs of UV cells when connected to a constant temperature bath. The machine had facilities for repetitive scanning of a selected region at a preselected time interval

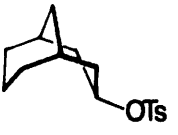
(adjustable from approximately 30 seconds to 15 minutes) and although the interlocking mechanism allowed four solutions to be measured in this way only one reaction at a time could be accurately monitored (cf. figure 8). If the machine were locked at constant wavelength (262 m) the UV absorption of one solution could be monitored continuously, or if the automatic interchange of cells and discontinuous repetitive scan mode were utilised, up to four reactions could be followed simultaneously.

Temperature Control.

The constant-temperature bath was filled with water and controlled by a "Tempco" thermostat (specified tolerance $\pm$ 0.03C°). Bath temperatures (20-55°C) were determined with a thermometer calibrated by the National Physics laboratory, accurate to approximately $\pm$ 0.02 C°. The constant-temperature bath maintained a flow of water through a special cell holder located in the UV spectrometer. A fine thermocouple inserted into the solvolysis reaction and converted to a cold junction and potentiometer enabled a check to be maintained on the reaction temperature. No significant temperature gradient was noted between the bath temperature and reaction temperature at 25° or 50°C but a temperature gradient of 1.5C° was noted at 80°C. The temperature control at 25° was satisfactory ($\pm$ 0.1C°) after equilabration, but deteriorated somewhat as the bath temperature was increased, and

at 80°C the temperature was only maintained ± 0.3C° for short periods, and evaporation losses became significant.





at 25°C

Acetolysis of EXO-bicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate

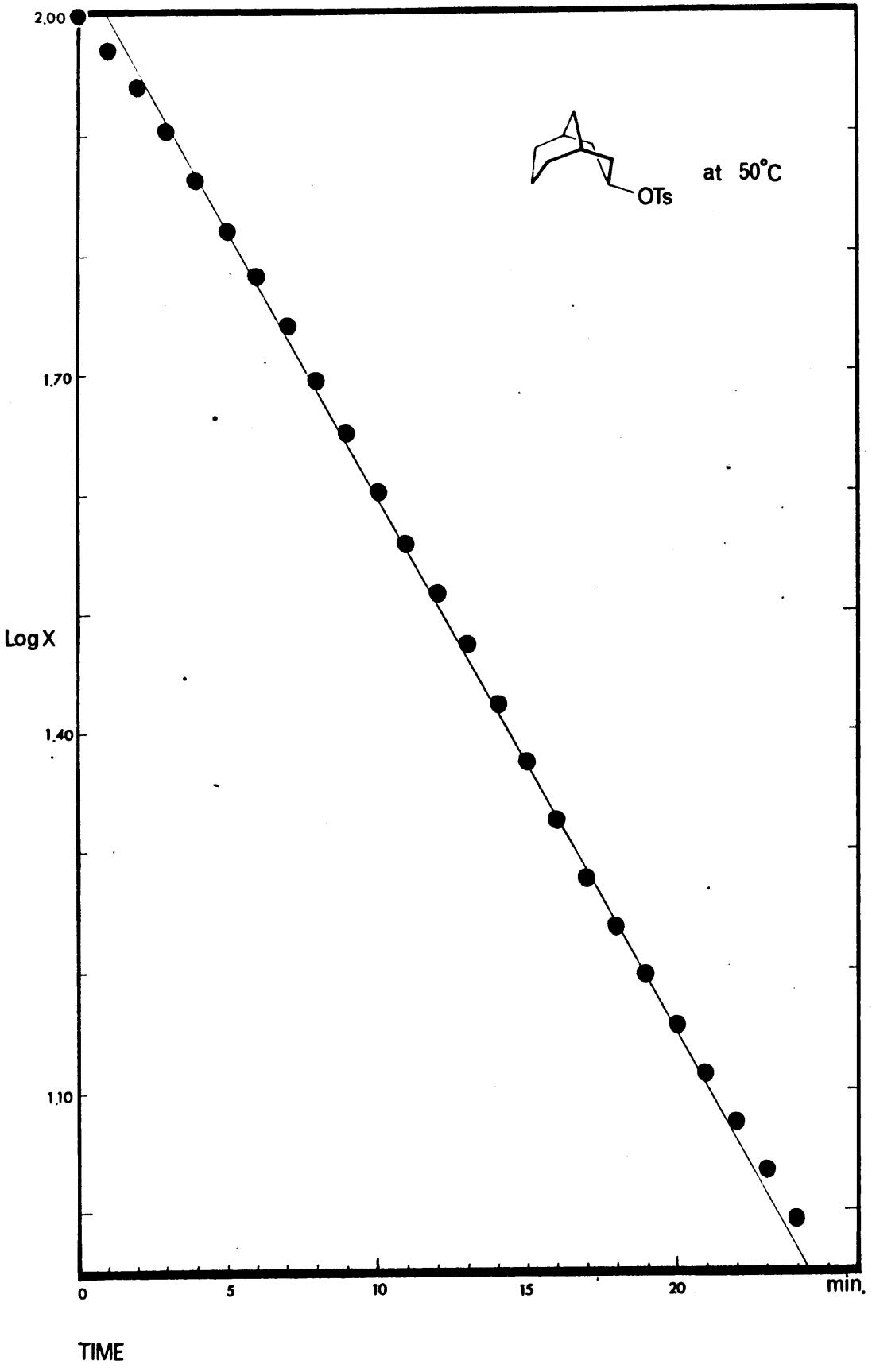
ROTs: 2.84×10^{-3}M. Temperature: 25.0°C(± 0.1)

NaOAC: 5.07×10^{-3}M. Scan Interval: 15 mins. 11 secs.

Scan.	Optical Density	X.	$Log_{10}X.$
0	1.560	100.0	2.000
1	1.530	94.6	1.9765
2	1.505	90.4	1.9565
3	1.480	85.9	1.934
4	1.460	82.5	1.9165
5	1.440	79.0	1.8975
6	1.415	74.6	1.873
7	1.390	70.2	1.8485
8	1.370	65.7	1.8245
9	1.350	63.1	1.8005
10	1.330	59.7	1.776
11	1.310	56.1	1.750
12	1.295	53.5	1.7285
13	1.280	50.9	1.707
14	1.265	48.3	1.684
15	1.250	45.6	1.6595
16	1.235	43.0	1.6335
17	1.220	40.4	1.606
18	1.205	37.75	1.577
19	1.190	35.1	1.5455
20	1.180	33.3	1.523
	0.990	0.	-

From graph opposite: $t_{\frac{1}{2}}$ = 200 mins.

$k_1 = 5.78 \times 10^{-5}$ sec^{-1}.


2.00
1.70
1.40
1.10
Log X
OTs
at 50°C
0
5
10
15
20
min.
TIME

Acetolysis of EXO-bicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate

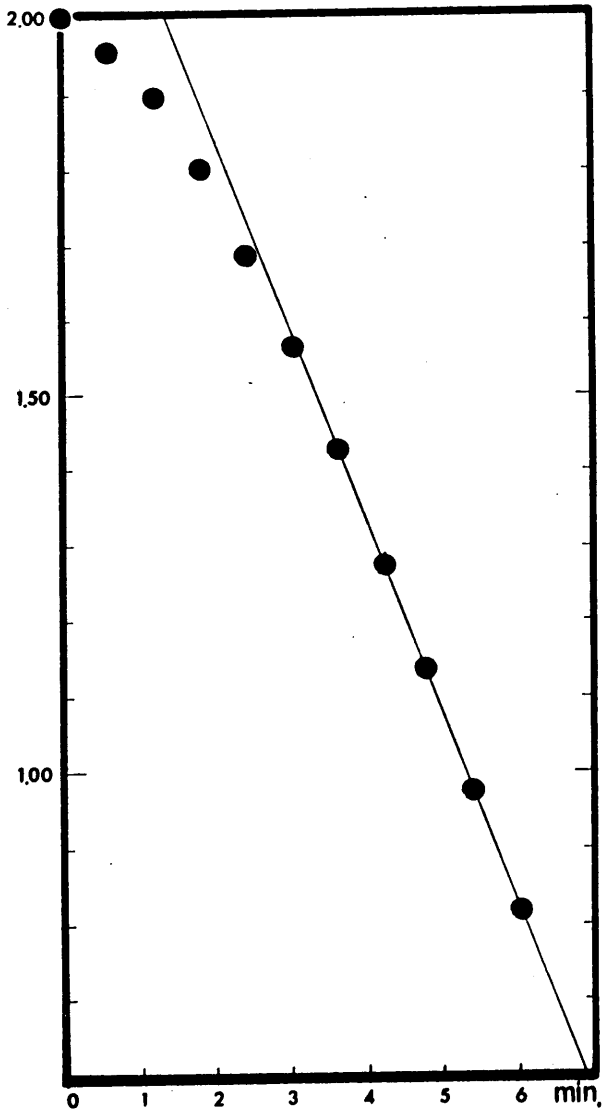
ROTs: 3.15×10^{-3}M. Temperature: 50.0°C(± 0.15)

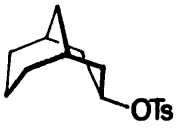
NaOAC: 5.07×10^{-3}M. Scan interval: 60 secs.

Time (mins.)	Optical Density	X.	Log_{10}X.
0	1.740	100.0	2.000
1	1.675	93.0	1.968
2	1.655	86.6	1.9375
3	1.610	79.6	1.9015
4	1.565	72.6	1.861
5	1.520	65.6	1.817
6	1.485	60.2	1.780
7	1.450	54.6	1.738
8	1.415	49.2	1.692
9	1.385	44.5	1.6485
10	1.355	39.8	1.600
11	1.330	35.9	1.5555
12	1.310	32.8	1.516
13	1.290	29.7	1.4725
14	1.270	26.8	1.4245
15	1.250	23.4	1.370
16	1.235	21.1	1.324
17	1.220	18.75	1.2735
18	1.210	17.2	1.236
19	1.200	15.6	1.194
20	1.191	14.2	1.1525
21	1.183	12.95	1.1125
22	1.176	11.9	1.074
23	1.169	10.75	1.032
24	1.163	9.85	0.993
	1.100	0.	-

From the graph opposite; $t_{\frac{1}{2}} = 10.1$ mins.

$k = 1.14 \times 10^{-3}$ sec^{-1}.





at 70°C

Acetolysis of EXO-bicyclo(3.3.1)nonanyl Toluene-p-sulphonate

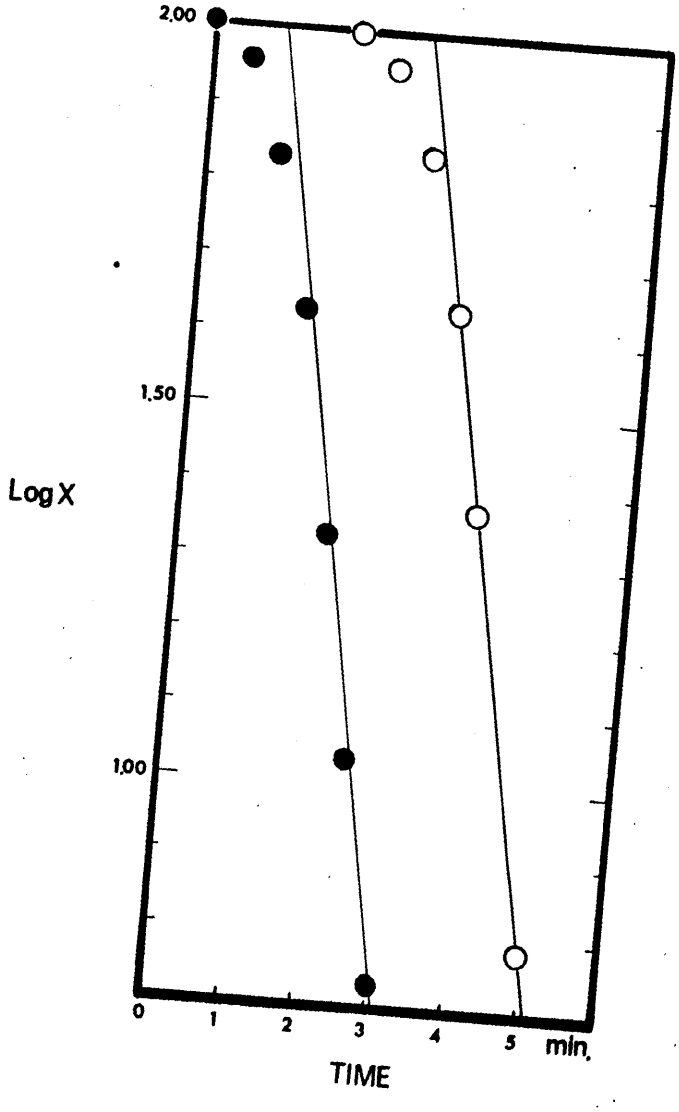
ROTs: 2.59×10^{-3}M Temperature: 70.0°C(± 0.25).

NaOAC: 4.26×10^{-3}M Scan interval: 36 seconds.

Time (mins.)	Optical Density	X.	$Log_{10}X.$
0	1.440	100.0	2.000
0.6	1.390	90.6	1.9575
1.2	1.325	78.5	1.895
1.8	1.242	63.0	1.800
2.4	1.165	48.6	1.678
3.0	1.100	36.4	1.5615
3.6	1.048	25.7	1.426
4.2	1.005	18.7	1.272
4.8	0.978	13.65	1.1355
5.4	0.955	9.35	0.971
6.0	0.940	6.55	0.816
6.6	0.928	4.3	0.634
7.2	0.920	2.8	0.448
	0.905	0.	-

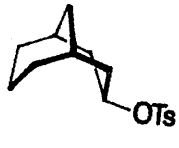
From graph opposite; $t_{\frac{1}{2}} = 1.25$ mins.

$k = 9.25 \times 10^{-3}$ sec^{-1}.



● Run A

○ Run B



at 80°C.

Acetolysis of EXO-bicyclc(3.3.1)nonan-3-yl Toluene-p-sulphonate

RUN A ROTs : 1.86×10^{-3}M Temperature : 80.0°C (± 0.3)

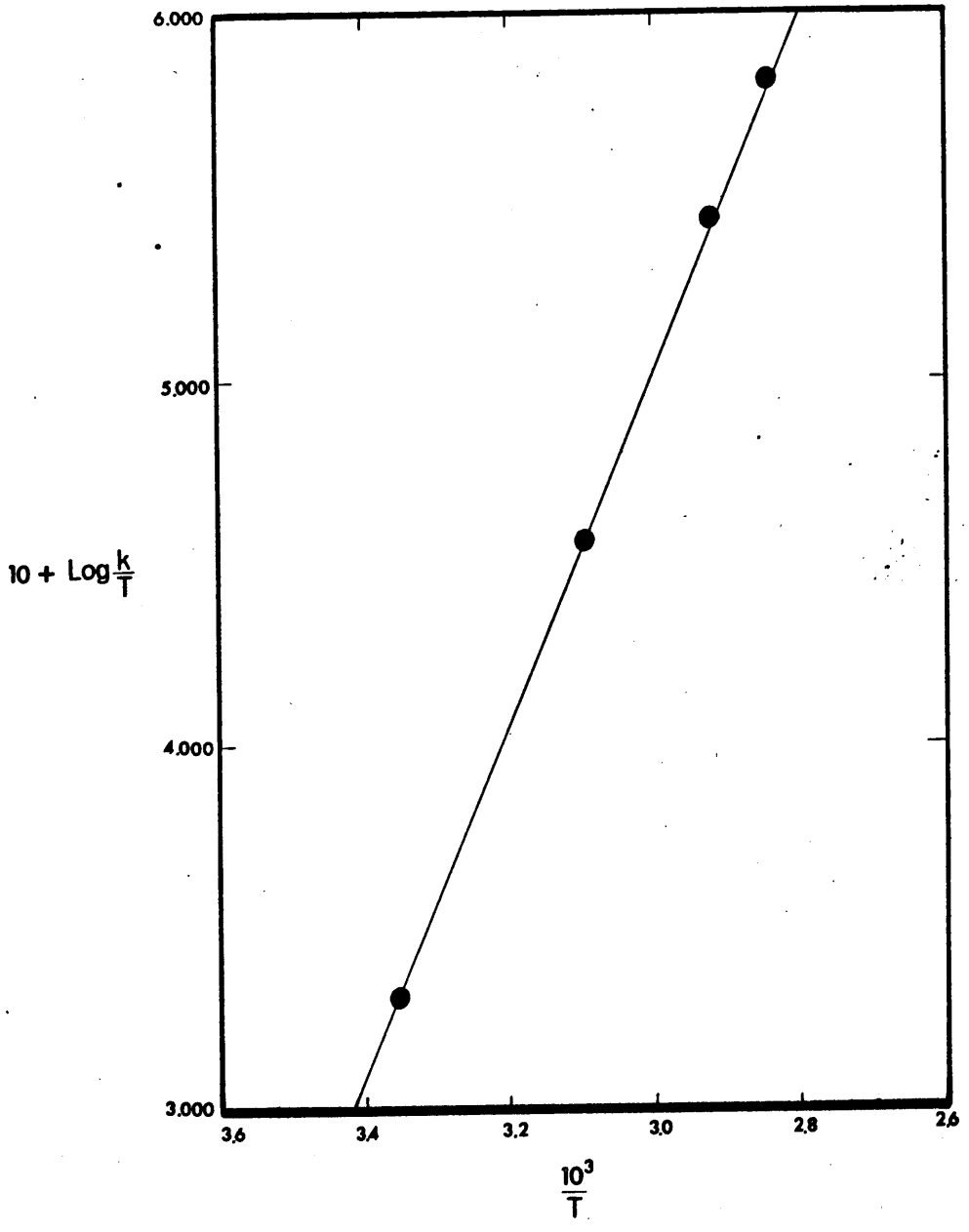
RUN B ROTs : 1.94×10^{-3}M

NaOAc : 3.50×10^{-3}M

	Time (mins.)	Optical Density	X.	Log_{10}X.
RUN A.	0.0	1.025	100.0	2.000
	0.5	0.990	90.6	1.958
	1.0	0.905	68.1	1.8335
	1.5	0.810	42.6	1.630
	2.0	0.730	21.3	1.329
	2.5	0.690	10.65	1.028
	3.0	0.670	5.32	0.7275
	10.0	0.650	0.	-
RUN B.	0.0	1.085	100.0	2.000
	0.5	1.040	89.1	1.950
	1.0	0.945	68.25	1.834
	1.5	0.850	42.6	1.6305
	2.0	0.770	22.0	1.365
	3.0	0.700	6.1	0.785
	3.5	0.685	2.2	0.346
	4.0	0.680	1.22	0.086
	10.0	0.675	0.	-

From graphs opposite; $t_{\frac{1}{2}}$ = 30.0 seconds.

$k = 2.31 \times 10^{-2}$ sec^{-1}.

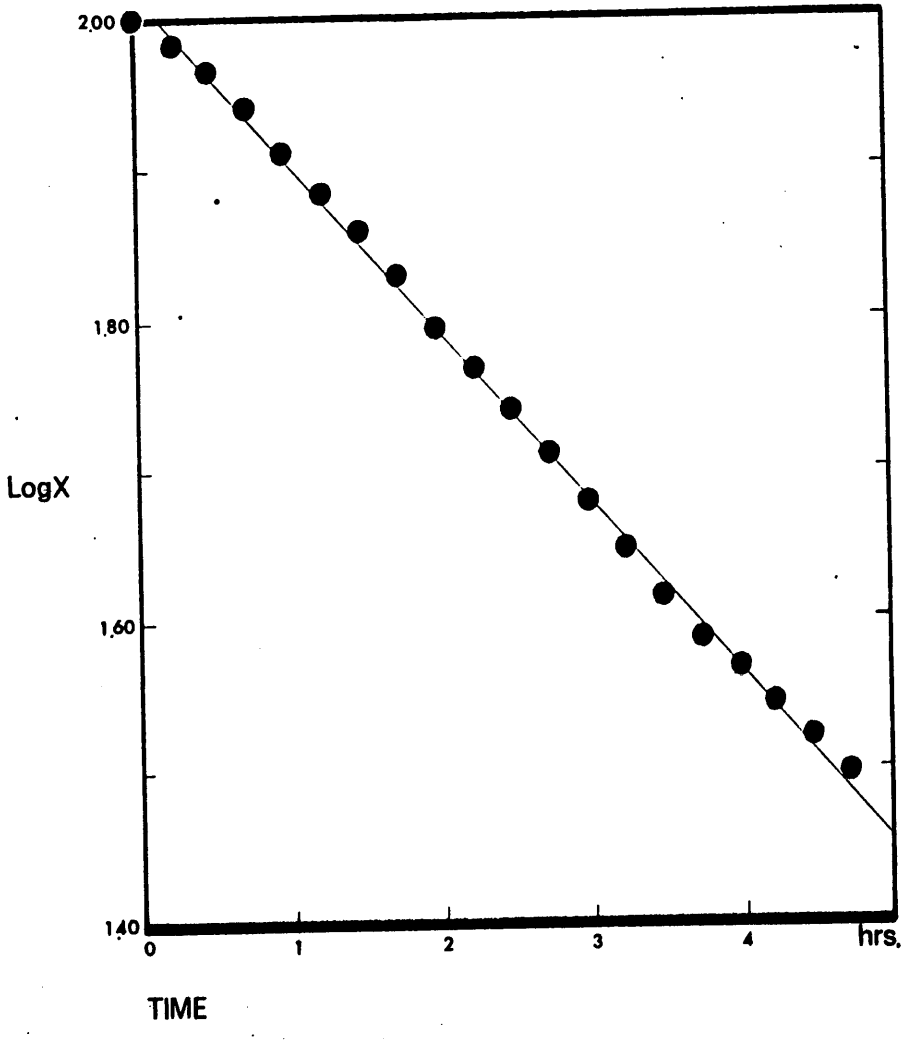

6.000
5.000
4.000
3.000
10 + Log k/T
3,6
3,4
3,2
3,0
2,8
2,6
10³/T

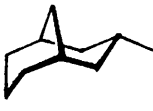
Enthalpy of Activation for the Acetolysis of 3-Exo-bicyclo(3.3.1)nonanyl Toluene-p-sulphonate (52).

Temperature °C.	Temperature °K.	k_1 (sec^{-1}.)	10 + log k/T	$10^3/T$
25	298	5.78×10^{-5}	3.287	3.355
50	323	1.14×10^{-3}	4.549	3.095
70	343	9.25×10^{-3}	5.428	2.919
80	353	2.31×10^{-2}	5.816	2.835

From the gradient of the plot of '10 + log k/T' versus '10 3/T' opposite,

$$H^{\ddagger} = 23.0 \text{ kcal/Mole.}$$





at 25°C

Acetolysis of ENDO-bicyclo(3,3,1)nonan-3-yl Toluene-p-sulphonate

ROTs: ca. 2.1×10^{-3}M * Temperature: 25.0°C(± 0.1)

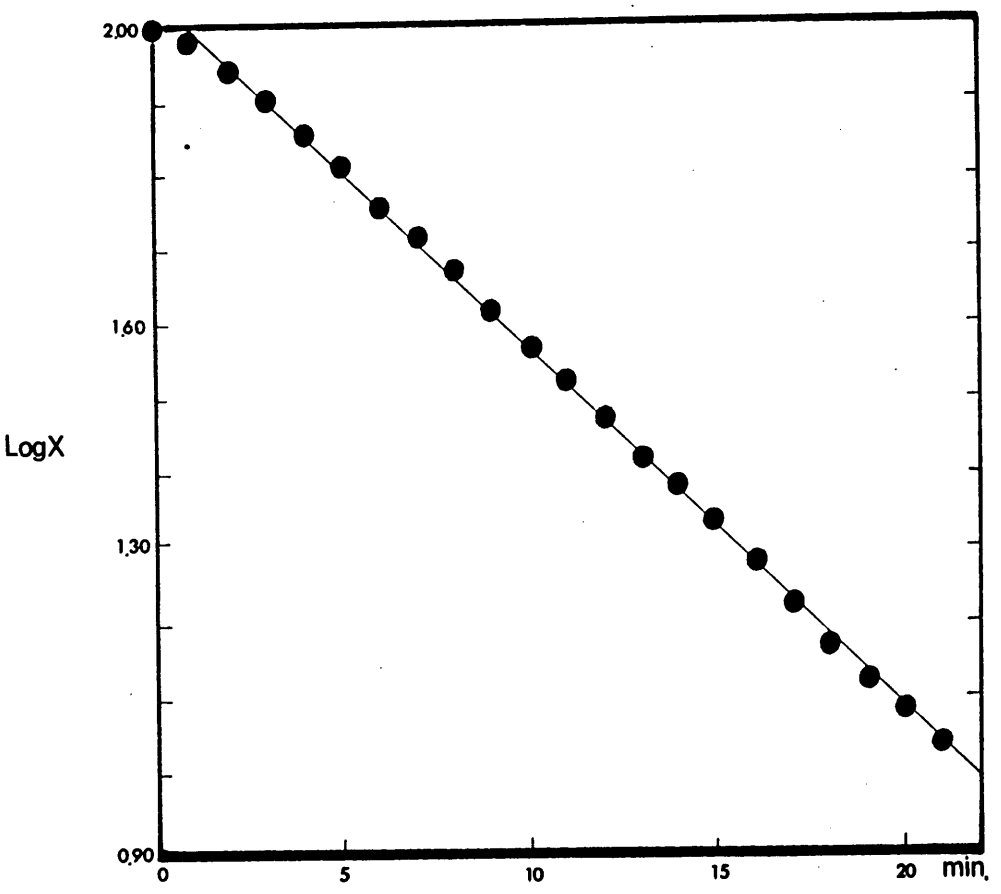
NaOAc: 4.38×10^{-3}M Scan interval: 15 mins.

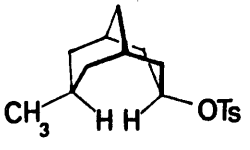
Scan.	Optical Density	X.	Log_{10}X.
0	1.165	100.0	2.000
1	1.155	96.4	1.984
2	1.145	92.9	1.968
3	1.130	87.4	1.942
4	1.115	82.0	1.914
5	1.100	76.5	1.884
6	1.090	72.6	1.862
7	1.075	67.6	1.830
8	1.060	62.1	1.794
9	1.050	58.5	1.768
10	1.040	54.9	1.740
11	1.030	51.3	1.711
12	1.020	47.6	1.678
13	1.010	44.1	1.645
14	1.002	41.2	1.615
15	0.995	38.7	1.587
16	0.990	36.9	1.567
17	0.985	35.0	1.544
18	0.980	33.2	1.522
19	0.975	31.4	1.498
	0.888	0	-

From graph opposite; $t_{\frac{1}{2}}$ = 160 mins.

k_1 = ca 7.36×10^{-5} sec^{-1}.

*This tosylate was an oil and contained 6-7% of its epimer.





at 50°C

Acetolysis of 7-EXO-methyl-3-EXO-bicyclo(3.3.1)nonanyl Toluene-p-sulphonate

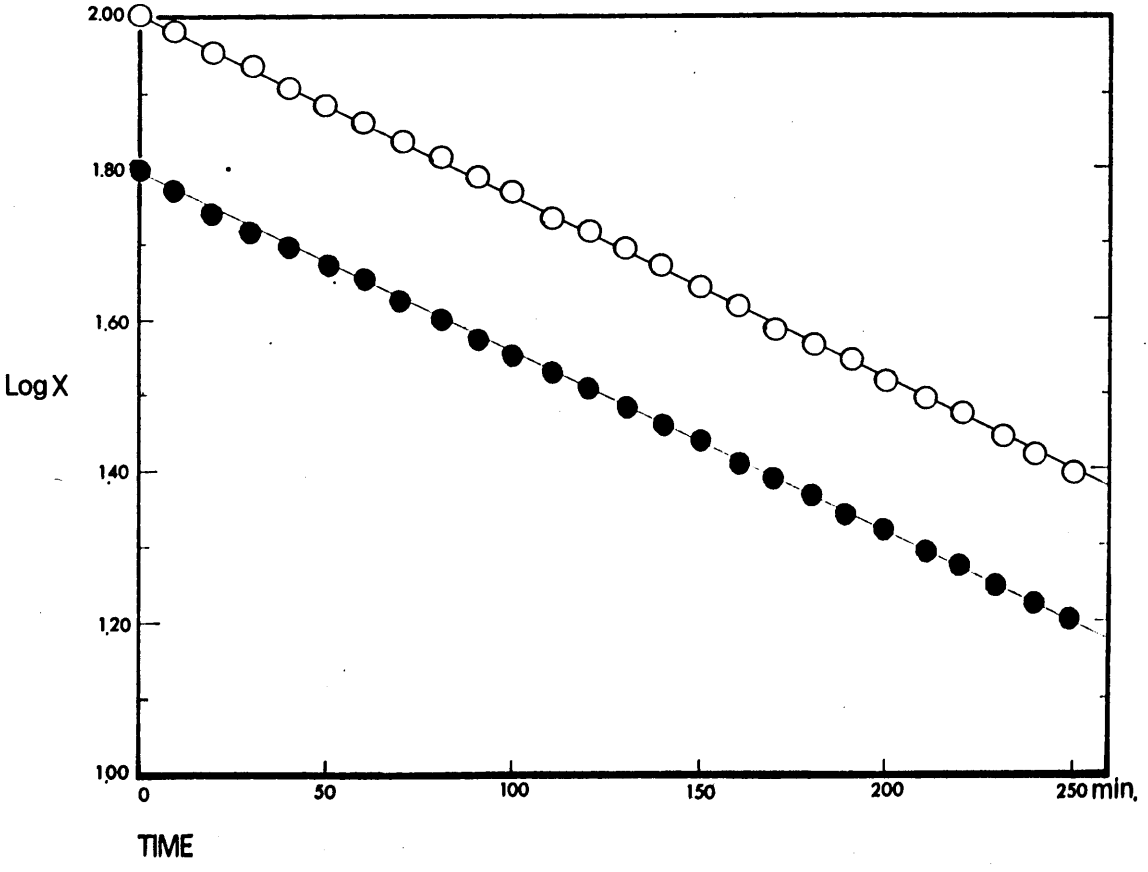
ROTs: 2.41×10^{-3}M. Temperature: 50.0°C(± 0.15)

NaOAC: 4.38×10^{-3}M. Scan interval: 60 secs.

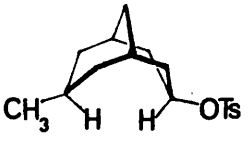
Time (mins.)	Optical Density	X.	Log_{10}X.
0	1.380	100.0	2.000
1	1.360	96.3	1.984
2	1.320	88.8	1.949
3	1.275	80.6	1.906
4	1.230	72.2	1.859
5	1.190	64.8	1.812
6	1.150	57.5	1.760
7	1.120	50.9	1.715
8	1.090	46.3	1.676
9	1.065	41.6	1.620
10	1.040	37.0	1.568
11	1.020	33.3	1.523
12	1.000	29.6	1.472
13	0.983	26.5	1.423
14	0.970	24.1	1.382
15	0.957	21.7	1.336
16	0.943	19.0	1.280
17	0.930	16.6	1.222
18	0.920	14.7	1.170
19	0.912	13.3	1.124
20	0.905	12.0	1.081
21	0.900	11.1	1.046
	0.840	0.	-

From graph opposite; $t_{\frac{1}{2}} = 6.20$ mins.

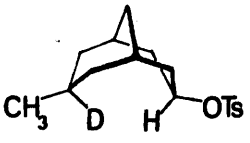
$k = 1.865 \times 10^{-3}$ sec^{-1}.


2.00
1.80
1.60
1.40
1.20
1.00
Log X
0
50
100
150
200
250 min.
TIME

○ **98**
● **99**
} at 25°C


CH3
H
H
OTs

,


CH3
D
H
OTs

Simultaneous Acetolysis of 7-Exo-methyl-3-exo-bicyclo(3.3.1)nonanyl and 7-Endo-deutero-7-exo-methyl-3-exo-bicyclo(3.3.1)nonanyl Toluene-p-sulphonates (98, 99).

98: 2.2×10^{-3}M. Temperature: 25.0°C (±0.1)

99: 1.3×10^{-3}M. Scan Interval: 10.0 mins.

NaOAc: 2.5×10^{-3}M.

(98) Log X	X	O.D.	Time	O.D.	X	Log X (99)
2.000	100.0	1.315	0	0.810	100.0	2.000
1.980	95.5	1.290	10	0.785	93.0	1.969
1.954	89.9	1.260	20	0.765	87.4	1.941
1.936	86.2	1.240	30	0.750	83.1	1.920
1.907	80.7	1.210	40	0.735	79.0	1.897
1.881	76.1	1.185	50	0.720	74.8	1.8735
1.860	72.5	1.165	60	0.705	70.5	1.848
1.838	68.8	1.145	70	0.692	66.6	1.8245
1.814	65.1	1.125	80	0.680	63.4	1.802
1.789	61.5	1.105	90	0.668	60.0	1.778
1.769	57.7	1.090	100	0.658	57.2	1.757
1.731	55.1	1.070	110	0.648	54.4	1.7355
1.719	52.3	1.055	120	0.638	51.6	1.712
1.695	49.9	1.040	130	0.628	48.7	1.688
1.670	46.8	1.025	140	0.618	45.9	1.662
1.644	44.1	1.010	150	0.610	43.6	1.640
1.616	41.25	0.995	160	0.602	41.5	1.6175
1.586	38.6	0.980	170	0.594	39.2	1.5935
1.565	36.7	0.970	180	0.587	37.2	1.571
1.542	34.8	0.960	190	0.580	35.2	1.547
1.519	33.0	0.950	200	0.573	33.2	1.522
1.494	31.2	0.940	210	0.567	31.6	1.4995
1.468	29.4	0.930	220	0.561	29.8	1.474
1.440	27.4	0.920	230	0.555	28.2	1.450
1.4195	26.2	0.913	240	0.550	26.8	1.427
1.394	24.8	0.905	250	0.545	25.4	1.404
1.3565	23.3	0.897	260	0.540	24.0	1.380
1.3435	22.0	0.890	270	0.535	22.5	1.352
1.317	20.8	0.883	280	0.530	21.1	1.3245
1.299	19.5	0.876	290	0.525	19.8	1.295
1.264	18.3	0.870	300	0.520	18.3	1.2625

continued.....

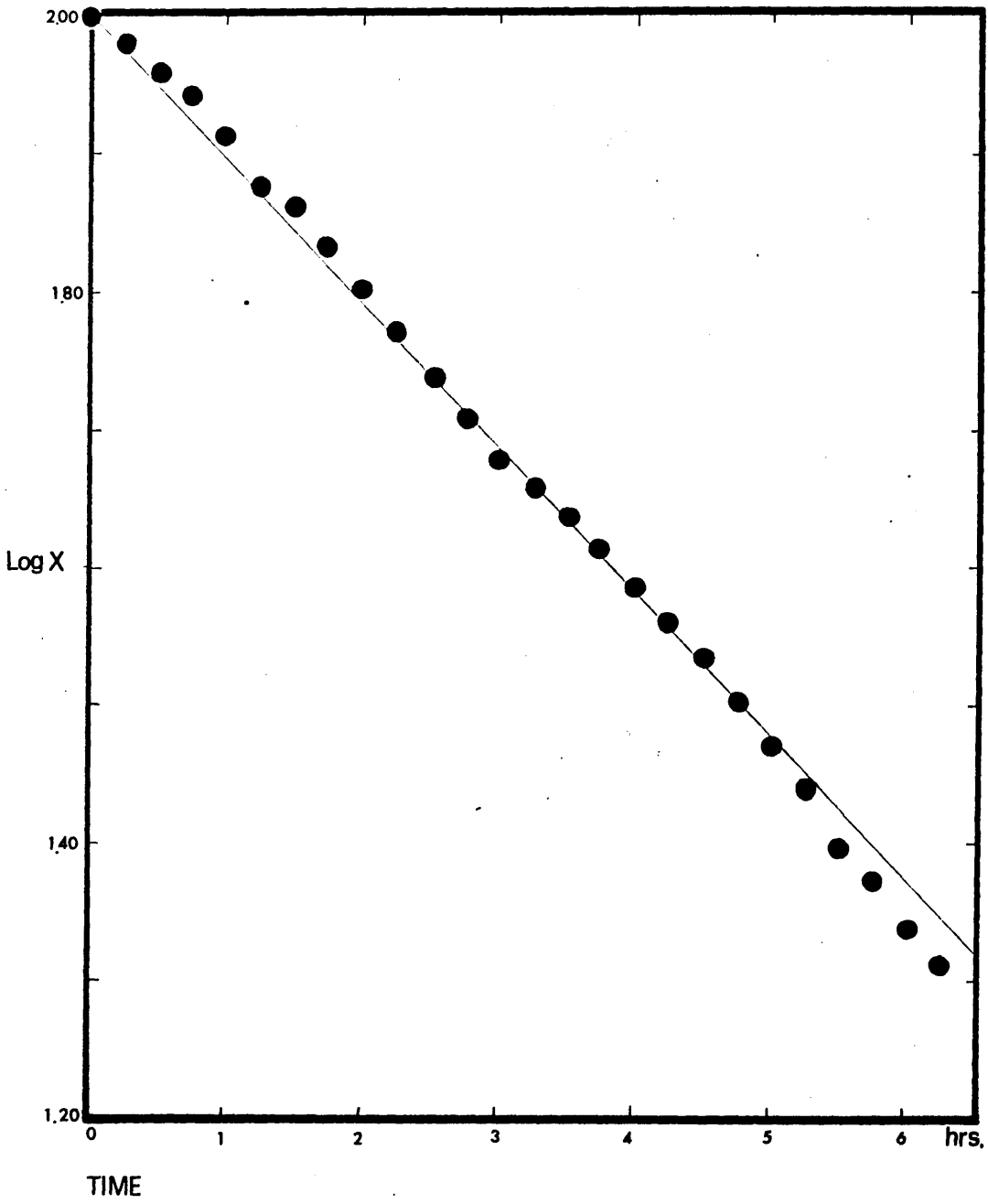
continued

1.241	17.3	0.865	310	0.517	17.45	1.242
1.218	16.5	0.860	320	0.514	16.6	1.220
1.193	15.6	0.855	330	0.511	15.8	1.198
1.167	14.7	0.850	340	0.508	14.9	1.174
1.139	13.8	0.845	350	0.506	14.3	1.157
1.114	13.0	0.841	360	0.504	13.8	1.140
1.090	12.3	0.837	370	0.502	13.2	1.122
1.0635	11.55	0.833	380	0.500	12.65	1.103
1.034	10.8	0.829	390	0.498	12.1	1.0835
1.004	10.1	0.825	400	0.496	11.5	1.062
0.989	9.7	0.823	410	0.494	11.0	1.0415
0.972	9.35	0.821	420	0.492	10.4	1.018
0.955	9.0	0.819	430	0.490	9.9	0.994
0.936	8.6	0.817	440	0.488	9.3	0.968
0.916	8.25	0.815	450	0.486	8.7	0.942
0.897	7.9	0.813	460	0.484	8.15	0.912
0.876	7.5	0.811	470	0.482	7.6	0.881
0.854	7.15	0.809	480	0.481	7.3	0.864
0.832	6.8	0.807	490	0.480	7.05	0.848
0.808	6.4	0.805	500	0.479	6.8	0.830
	0.0	0.770		0.455	0.0	-

From graphs; $t_{\frac{1}{2}}$ = 125 mins. $t_{\frac{1}{2}}$ = 125 mins.

$K_H = 9.25 \times 10^{-5} sec^{-1}$ $K_D = 9.25 \times 10^{-5} sec^{-1}$

Table 10 refers.



CYCLOHEXYL TOSYLATE AT 78.5°C

Acetolysis of Cyclohexyl Toluene-p-sulphonate

ROTs: 2.15×10^{-3}M. Temperature: $78.5^{\circ}C(\pm 0.3)$

NaOAc: 4.38×10^{-3}M. Scan interval: 15 min. 10 sec.

Scan	Optical Density	X.	$Log_{10}X.$
0	1.190	100.0	2.000
1	1.170	95.5	1.980
2	1.150	91.0	1.959
3	1.130	86.4	1.9365
4	1.110	81.9	1.913
5	1.080	75.0	1.875
6	1.070	72.6	1.862
7	1.050	68.2	1.834
8	1.030	63.6	1.8035
9	1.010	59.1	1.772
10	0.990	54.5	1.738
11	0.975	51.2	1.709
12	0.960	47.7	1.679
13	0.950	45.5	1.658
14	0.940	43.2	1.6355
15	0.930	40.9	1.612
16	0.920	38.6	1.587
17	0.910	36.4	1.561
18	0.900	34.1	1.533
19	0.890	31.8	1.503
20	0.880	29.5	1.470
21	0.870	27.2	1.436
22	0.860	25.0	1.398
23	0.853	23.4	1.370
24	0.846	21.8	1.339
	0.750	0.0	-

From graph opposite; $t_{\frac{1}{2}} = 175.5$ minutes

$k = 6.58 \times 10^{-5}$ sec^{-1}.

GLC DATA

COMPOUND	COLUMN	TEMP.	FLOW RATE	RET. TIME (OR INDEX).
3	20% TCEP	50°C	55ml/min.	9.1 min.
22	"	"	"	8.4
25	"	"	"	7.4
26	"	"	"	10.0
22	10% Ap L	100°C	50	8.5
25	"	"	"	9.6
119	5% QF 1.	100°C	24	18.3
120	"	"	"	21.4
123	"	"	"	21.4
124	"	"	"	21.4
125	"	"	"	19.2
30	5% Carbowax	125	45	11.5
31	"	"	"	12.4
39	"	"	"	11.5
42	"	"	"	12.4
103	"	"	"	6.2
126	"	"	"	10.5
127	"	"	"	9.7
128	"	"	"	9.7
22	10% ApL	125°C	50	1080
25	"	"	"	1095
30	"	"	"	1275
31	"	"	"	1305
39	"	"	"	1275
42	"	"	"	1305
79(X=H)	"	"	"	1235
79(X=Cl)	"	"	"	1365
79(X=OH)	"	"	"	1375
79(X=Br)	"	"	"	1480
103	"	"	"	1300
119	"	"	"	1335
120	"	"	"	1360
121	"	"	"	1370
122	"	"	"	1380
123	"	"	"	1350
124	"	"	"	1350
125	"	"	"	1335

Transannular Participation in the Bicyclo(3.3.1)nonane System.

INTRODUCTION

The phenomenon of "neighbouring group participation" [55,67] in the course of solvolytic reactions has been extensively studied in the last two decades. Participation of a functional group distant from the reaction site may influence the reaction by stabilising a transition state or intermediate by means of full or partial bonding to the reaction centre. This event may be manifest by a marked increase in rate over that observed in the absence of the neighbouring group and it is said to provide "anchimeric assistance" [68] to ionisation. Substrate stereochemistry is often a critical factor in such participation and marked stereospecificity in product formation is associated with such solvolytic reactions.

Neighbouring group participation is associated in numerous cases with the presence of oxygen, nitrogen or sulphur atoms, although the participation of carbon atoms has been demonstrated. When discussing the latter it is convenient to differentiate between alkyl (σ) and double bond (π) participation although the involvement of a cyclopropyl ring may lead to participation of an intermediate nature.

Sigma bond participation, causing anchimeric assistance and stereospecific product formation, has been convincingly

demonstrated by the work of Winstein et al. [69] using the norbornyl system as a simplified model of the monoterpene system in which this type of participation was first demonstrated [70]. The volume of work related to this topic is enormous and a more detailed account is outwith the context of this thesis, however several leading review articles discuss in depth the arguments of Brown, Winstein and many others who have contributed towards establishing the precise nature of the intermediates involved in alkyl participation.[71,72]

Double bond ( )-participation, for the purposes of this thesis may be subdivided into 3 distinct types on the basis of the relative insulation of the double bond from the potential cationic centre. It is well established that allylic derivatives in which the bouble bond is - to the potential cationic centre, are much more reactive than their saturated analogues in solvolytic reactions, and the intermediate ion is considered to have marked stabilisation from delocalisation of the -electrons of the double bond.[73]

There are many examples of homo allylic participation in which one saturated carbon atom intervenes between the double bond and the potential carbonium ion. One of the earliest and surely one of the most striking examples was discovered by Shoppee [74], and later studied in detail by Winstein [75] involving -participation in solvolysis of 3-cholesteryl tosylate (1). Shoppee found that substitution

reaction of 3-cholesteryl derivatives gave products whose configuration was the same as that of the starting compound. Treatment of 3-cholesteryl compounds in buffered solvents gave i-steroids also with the -configuration (2) [75]. Since cholesteryl tosylate (1) also solvolysed faster than cholestanyl tosylate (factor of 40 at 70°C) Winstein proposed that the non-classical ion 3 was the intermediate formed in solvolysis. Later work by Shoppee [76] showed that 3-cholesteryl derivatives also solvolyse faster than 3-compounds which eliminate to give the diene.

The interconversion of the homoallylic and cyclopropyl carbinyl systems 1 and 2 is critically dependent on the stereochemistry of the leaving group in 1, however it has been shown that both epimeric 3,5-cyclocholestan-6-yl chlorides (2,7 X = Cl) afford 3-cholesteryl products on solvolysis [77], thus the stereochemical requirements for cyclopropyl participation appear to be less demanding in this system. If the unsymmetrical intermediates 3 and 5 were involved in the solvolysis of the 6 and 6 compounds (2 and 7) respectively, Winstein has argued that there should be a large difference in the reaction rates in favour of the 6-compound and the finding of a rate ratio, $k_2/k_7 = 10$ is evidence of the intermediacy of 4 [78].

More recently, Whitham [79], solvolysed the tosylate of 3-hydroxymethyl-A-norcholest-5-ene (6, X = OTs) in aqueous

acetone buffered with potassium acetate. This produced a mixture of alcohols 1 and 2 (X = OH) in the same ratio as that formed in the solvolysis of cholesteryl tosylate under the same conditions, favouring the symmetrical ion 4 as the common intermediate.

Probably the most famous example of homoallylic participation is to be found in the acetolysis of anti-7-norbornenyl tosylate (8) which produces exclusively anti-7-norbornenyl acetate (10) with a rate 10^{11} times faster than that observed for the saturated analogue [80]. Winstein proposed that 9 was a suitable representation of the intermediate formed and that the remarkable increase was due to the developing charge being stabilised by delocalisation of the double bond forming a symmetrical bis-homocyclopropenyl cation. The rate of acetolysis of the epimeric syn-7-norbornenyl tosylate on the other hand, was significantly slower, by a factor of 10^7, but still some 10^4 times more reactive than the saturated compound. The product obtained from solvolysis proved to be ^{2}-bicyclo(3,2,0)hepten-4-ol (13) and in this instance the participation is considered to involve a C-C bond of the anti 5-membered ring (11) producing the stabilised allylic cation 12.

A considerable number of investigations have been carried out to determine the steric requirements necessary for the overlap between a double bond and a developing homoallylic

carbonium ion. The results obtained by DePuy et al.[81] in the acetolysis of the exo- and endo-7-isopropylidene-dehydro-norbornyl tosylates are informative in this context. The exo-tosylate 14 is considered to ionise in an assisted manner to give the homoallylic ion 15, which is symmetrical with respect to the norbornyl double bond [82] and affords the acetate 16 in a stereospecific manner. That marked stereo-specificity is associated with double bond participation can be seen in the solvolysis of the endo-tosylate 17, which proceeds with total retention of configuration without rearrangement to afford 19 via the homoallylic cation 18 in which the 7-isopropylidene double bond participates in an assymetric manner.

The third Sub-group of π-participation, in cyclic systems in which several carbon atoms intervene between the potential cation and the double bond, may be termed transannular participation. Such participation has been clearly demonstrated in the 10 membered aliyclic ring. In 1956, Goering et al.[83] observed ring closure when 6-ketocyclodecyl tosylate (20) was solvolysed, and suggested that the product bicyclo(5,3,0) decan-2-one (22) was formed by transannular participation of the double bond present in the enol form 21. In subsequent investigations [84] the authors demonstrated that cis-5-cyclo-decen-1-yl tosylate (23, X = OTs) was some 10^4 times more reactive in acetolysis at 25° than cyclohexyl tosylate and the

production of the cyclised acetate (25, X = OAc) in a stereospecific manner is evidence in favour of anchimeric assistance of the double bond. Trans-5-cyclodecen-1-yl tosylate was too reactive to prepare and for this reason Goering and Closson [85] studied the solvolysis of the p-nitrobenzoate esters (23 and 26, X = OpNB) in aqueous acetone at 100°C. The trans compound 26 was shown to be 300 times more reactive than the cis-p-nitrobenzoate 23, inferring very efficient anchimeric assistance in the trans ester which produced the alcohol 28 (X = OH) in a stereospecific manner, as the major product. These results may be interpreted as involving the non-classical ions 24 and 27 respectively.

One particular aspect of transannular double bond participation has received considerable attention, for in certain systems double bond participation can stabilise a potential primary carbonium ion with the formation of a cyclic product. Such participation was first demonstrated in 1961 by Mdme. LeNy who subjected 4-cyclooctenyl methyl brosylate (29) to acetolysis and produced 2-endo-bicyclo(3,2,1)octyl acetate (31, X = OAc, 90%) in high stereospecificity with a rate enhancement of 30 compared with the saturated compound [86]. This result has been explained in terms of the bridged non-classical ion 30, which is also considered to be an intermediate in the solvolysis of 2-endo-bicyclo(3,2,1)octyl tosylate (31, X=OTs) [87]. Winstein had designated two such

routes to the same bridged cation the - and - routes respectively, and has shown 2-(cyclohex-4-enyl)ethyl brosylate (32) is similarly related to 2-bicyclo(2,2,2)octyl and 2-exo-bicyclo(3,2,1)octyl acetates (34 and 35, X = OAc) which are produced in 80% yield in acetolysis. The solvolysis of 34 and 35 (X = OTs) constitute different -routes to the same ion 33, and 32 represents the -route [88].

Cope[89] has shown that there is no evidence to suggest that anchimeric assistance occurs in the solvolysis of 4-cycloocten-1-yl brosylate (36); the rate of acetolysis is of the same order as cyclohexyl brosylate (a rate factor of 2.9 at 25°C) and the solvolysis products, outlined in Scheme 1, are indicative of the intermediary of classical ions rather than a single bridged non-classical ion. In contrast with these results, Leal and Pettit [90] have shown that in the bridged nine-membered ring present in 37 the involvement of the double bond can be domonstrated in a novel manner. When the cis-fused phenyl carbinol 37 or the corresponding olefin 38, is dissolved in strong acid, the solutions have the same anomolous ultra-violet absorption, absent in the case of the trans-fused compounds and this has been interpreted as evidence of the presence of the bridged non-classical intermediate 39.

Winstein [91] has investigated the solvolysis of an analogous system in which the nine-membered ring is further

constrained, as a result the attitude of the double bond to the leaving group is unusual (40). That there is considerable anchimeric assistance to ionisation has been demonstrated for the brosylate 40 is some 10^{11} times more reactive than the 7-norbornyl derivative, and only some 4 times less reactive than the anti-7-norbornenyl compound (8). The non-classical intermediate 41, which may represent a unique homocyclopropenyl cation adequately accounts for the formation of both acetate 42 (X = OAc), and by internal return, brosylate 42 (X = OBs).

Even greater reactivity was associated with the half-cage derivatives, 43, [92] and the trifluoroacetate rather than the brosylate derivative was prepared. The rate of solvolysis of 43 ($X = OCOCF_3$) in aqueous acetone was found to be 13 times greater than the corresponding anti-7-norbornenyl derivative, and the absence of unsaturated products is in accord with anchimeric assistance in the course of ionisation. The reactivity of the half-cage derivative 43 can be related to the exo norbornyl system, and is some 200 fold more reactive. The main products of solvolysis **48** (34%), **49** (43%) and the "bird-cage" hydrocarbon **47** (41%) can be derived from three product-forming intermediates, and it is of interest that the initially formed cation **45**, is subject to two distinct internal rearrangements leading to **44** and **46** as shown.

Cyclopropyl participation in the course of solvolysis can likewise be subdivided with respect to the relative position of the potential carbonium ion; into cyclopropyl carbinyl systems, homocyclopropyl carbinyl systems and those further removed, in which transannular participation would be involved. There is evidence that the cyclopropyl carbinyl system itself represents a particular case of cyclopropyl participation. [93,94]

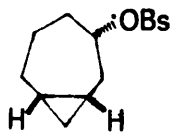
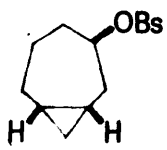
Substituted cyclopropyl carbinyl systems have been investigated and have been found to be more reactive than the homoallylic compound to which they are related e.g. the case of the i-steroid-cholesteryl rearrangement [78]. This order of reactivity was not observed in the nortricyclyl-2-norbornenyl system [95], 50-~~51~~ 52, and there is little evidence to support the symmetrical ion ~~52~~ 51 as an exclusive highly stabilised intermediate [96].

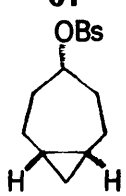
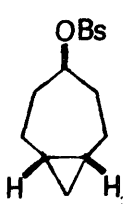
Cope [97] has investigated the cis- and trans- cyclopropyl carbinyl systems 53 and 54 and has observed that they are more reactive than the homoallylic system 55. It had been shown that 3-cycloocten-1-yl brosylate (55, X = OBs) was more reactive in acetolysis than cyclohexyl brosylate by a factor of 370 at 70°C and the contention that ionisation was assisted was supported by the product analysis, which gave only acetates 55, 54 and 53 (X = OAc) the latter being the major products [89]. The intermediate was formulated as

56, which might be expected to furnish cis acetate (53) in an exclusive manner, but that both cis and trans acetates (53 and 54, X = OAc) were produced was established in a later paper,[98] and this may be evidence of the intermediary of 57. The cyclopropyl carbinyl brosylates (53, 54 X = OBs) were too reactive to prepare, but the trifluoroacetate derivatives were studied. The solvolysis of 53, 54 or 55 ($X = OCOCF_3$) in acetic acid resulted in the interconversion of each of these systems without the production of olefin and it is perhaps significant that the enhanced rate of solvolysis of both cis and trans-cyclopropyl carbinyl derivatives indicates effective anchimeric assistance.

Homocyclopropyl participation was first investigated by Winstein's group in 1959, who studied the acetolysis of cis- and trans-3-bicyclo(3,1,0)hexyl tosylates (58 and 59).[99] The trans-tosylate 59 afforded cis- acetate (67%) accompanied by elimination products (33%) which were not investigated further. The cis-tosylate 58 solvolysed with total retention of configuration to give only the cis-acetate. Deuterium labelling studies of the cis-tosylate in which the deuterium was (a) initially at C_3 alone, and (b) at both C_1 and C_5, showed that solvolysis was attended by a statistical distribution of deuterium among positions 1,3 and 5 in both (a) and (b). Solvolysis of the trans-tosylate specifically deuterated at C_3 under similar conditions was

TABLE 11

	A	B	C	D	E
64 	18	58	17	7%	–
 65	71	11	–	–	19%

	F	G	H	J
61 	70	4.5	25	0.5%
 62	43	44	13%	–

accompanied by only 7% deuterium redistribution. The rate enhancement of cis:trans is of the order of 40 and the demonstration of a special salt effect operative only in the solvolysis of the cis compound all support the intervention of a non-classical intermediate in the course of solvolysis of the cis-tosylate. Winstein proposed the tris-homocyclopropenyl cation 60 although Corey has argued that a set of equilibrating intermediates of lower symmetry could adequately explain the results. [100]

Attempts to prepare the tris-homocyclopropenyl cation by alternative routes, the deamination of the appropriate amines [100] and the oxidative decarboxylation of the corresponding carboxylic acids [101] were notably unsuccessful, but there remains no doubt that the data discussed above represents a detailed account of the course of acetolysis of the cis- and trans-tosylates [102]. The homo-cyclopropyl carbinyl system may be considered as transannular participation for orbital overlap as in 60 may be the process by which a cyclopropane ring may stabilise a potential transannular carbonium ion.

Transannular cyclopropyl participation in the bicyclo-(5,1,0) octyl system was subsequently investigated by Cope [97] who prepared the cis and trans pairs of 4- and 3-bicyclo(5,1,0) octyl brosylates (61,62,64 and 65). The products of acetolysis of 61 and 62 (Table 11) clearly suggest the intermediacy

of the classical 4-cation, particularly in olefin formation (F) and the net predominance of inverted acetate (H and G respectively), thus in the absence of kinetic data to support anchimeric assistance it must be assumed that the related non-classical ion 63 is not involved. On the other hand the solvolysis of 64 and 65 may proceed through a non-classical ion similar to 66 which can account for the stereospecificity of products A and B (table 11) by the interaction of acetate ion on 66 (a and b respectively), but such an intermediate does not account for the products C, D and E. That C and D are produced from the cis-brosylate 64 exclusively, and E from the trans-brosylate 65 indicates a marked product-dependence on configuration. The authors have suggested that B, C and D may arise via the intermediary pf the classical bicyclo-(3,3,0)octyl 3-cation (67) affording B and C directly and D in a specific manner via a 1,2 hydride shift. The absence of 3-exo bicyclo(3,3,0)octyl acetate from the products is in contradiction with earlier arguments [89] (see scheme 1). An alternative explanation assumes that the cis-brosylate (64) exists in a preferred conformation 68 (X = OBs) in which the leaving group is -equatorial. Attack of acetate ion on such a conformation (Figure 10) at C_2 from above the molecular plane may afford D in a concerted process involving a C_2C_1-hydride shift, cyclopropyl participation and ionisation, whereas C might result from a concerted elimination process

in which the axial C_2 proton is abstracted by acetate ion from below the molecular plane. The authors explain the formation of E from the trans brosylate 65 in a similar concerted process [97] but the conformation involved may be as shown in 69 (X = OBs): specific endo acetate attack at C_6, concerted with a C_6C_7 hydride shift, cyclopropyl participation and ionisation can be seen to account for the stereospecificity of the formation of E (Figure 10).

Whilst the mechanisms outlined above are tentative, the overall participation of the cyclopropane ring is indicated from the products of both cis- and trans-3-bicyclo-(5,1,0)octyl brosylates whereas there appears to be insignificant cyclopropyl participation in the isomeric cis- and trans-4-bicyclo(5,1,0)octyl brosylates (product J, table 11, may arise from endo acetate attack at C_1, cyclopropyl participation with C_3, accompanied by C_3C_4 hydride transfer and ionisation; Figure 10). Thus cyclopropyl participation may be critically dependent on the transannular distance of the carbonium ion.

As yet it is not possible to define completely the steric requirements for maximum participation of double bonds and cyclopropane rings, nor to assess the relative efficiency of the anchimeric assistance resulting from the participation of these functional groups. Hofmann [103] has carried out extended Hückel calculations to compare the efficiency of

double bond (71) and cyclopropyl stabilisation (72) of the theoretical cation 70 and showed that greater stability was associated with overlap of the cyclopropyl orbitals with the carbonium ion when similar distortions were allowed in each case.

We were interested in the possibilities for transannular participation inherent in the semi-rigid bicyclo(3,3,1)nonane system for in spite of our findings in Section I of no effective participation in the saturated system a suitably substituted system might exhibit unusual properties and enable us to compare the relative reactivities of double bond and cyclopropyl participation at the same site. An added incentive to such an investigation was the possibility of realising a -route to bridgehead carbonium ions, principally the 1-adamantyl cation for this has recently been the subject of considerable investigation.

Bridgehead 1-adamantyl compounds (73) are reactive compared with 2-substituted adamantyl compounds (a factor of 10^5) [104] and other bridgehead derivatives, notably 1-bicyclo-(2,2,2)octyl (74) and 1-norbornyl compounds (75). It was thought that some unique stabilising influence was operative in the case of the 1-adamantyl carbonium ion; hyperconjugative effects were suggested in which 3 equivalent mesomeric species provided stabilisation (76) [105] but this was discounted since the rate of solvolysis of the 3,5,7-trimethyl

compound (77, X = Br) was not enhanced relative to the tris-normethyl compound (73, X = Br) but was found to be somewhat slower.[106] A unique possibility exists in the 1-adamantyl carbonium ion for stabilisation; the vacant p-orbital at C_1 extending into the interior of the molecule may overlap with the backside orbital lobes of the sp^3 hybridised C-H bonds on the remaining three bridgehead positions all of which are directed toward the centre of the molecule (78)[107]. Experimental evidence in support of this concept is the abnormally low chemical shift of the bridgehead hydrogens in the 1-adamantyl cation (79) observed in strongly acidic solution.[108]

In view of the effects of transannular 3,7 methylene crowding in the solvolysis of 3-exo-bicyclo(3,3,1)nonanyl tosylate, we were interested in the 7-exomethylene and 7-cyclopropyl substituted compounds to compare their reactivity and the extent of transannular participation with that found in section I.

Our investigations in transannular reactions were linked with attempts to prepare specifically deuterated compounds as described in section I. The preparation of 7-exomethylene-bicyclo(3,3,1)nonan-3-one (80) has been described by Stetter [109,110], and the synthetic route is shown in Scheme 2. The ultra-violet (UV) spectrum of 80, λ_{max} 212 m , ε = 2600 in cyclohexane, is of interest since it is similar to the UV spectrum of trans-5-cyclodecenone which contains a solvent-dependent band (λ_{max} 214.5 m , ε = 2300 in 2,2,3,3,-tetra-fluoropropanol) assigned to the photodesmotic transition shown in 81, [111] whereas the UV spectrum of cis-5-cyclo-decenone (82) does not contain this band. Those spectral characteristics have been correlated with the relative reactivities of the cis and trans-5-cyclodecen-1-yl derivatives (23 and 26), for the trans-compound was found to be more reactive by a factor of 300 at 120°C [85]. The electronically exited state corresponding to the photodesmotic transition of the exomethylene ketone 80, may be represented by 83 or

possibly 84.

The chemical behaviour of the exomethylene ketone is unusual insofar as it was found extremely difficult to modify either of the functional groups without the intervention of transannular participation, notable in such reactions as catalytic hydrogenation which gave as the main product a tertiary alcohol, tentatively identified as 1-adamantanol. Reduction of the ketone 80 by methods other than lithium aluminium hydride was apparently invariably accompanied by transannular participation, although two distinct processes appear to be involved.

Sodium - moist ether reduction of the exomethylene ketone produced a tertiary alcohol assigned the structure 85 on the basis of the NMR spectrum which showed a methyl group at 9.0 and no signal in the region below 7.60. This was only the second time that the nor-adamantane ring system had been synthesised.[112] The formation of 85 is clearly dependent of the presence of the exomethylene group (86) for in the analogous system 87, Ayer and Piers effectively reduced the carbonyl function with lithium in liquid ammonia without any transannular involvement [21], yet the relative juxtaposition of the trigonal C_7 atoms to the carbonyl function must be comparable. In the exomethylene case however a primary carbanion may be produced (86) whereas such participation in 87 would lead to a secondary

carbanion thus transannular participation of this type may be specific to exomethylene groups.

A similar explanation may account for the product obtained from Wolff-Kishner reduction of the exomethylene ketone 80, since the hydrocarbon was incompatible with the required product, 3-exomethylenebicyclo(3,3,1)nonane. It was originally considered to be adamantane [112] but subsequent study showed that this assignment was in error for the GLC behaviour of the hydrocarbon was not identical with the latter on several columns, and the NMR spectrum showed a sharp singlet at 8.85 integrating for 3 protons consistant with the methylnoradamantane 88. Possible intermediates in the formation of 88 are the carbanions 89 and 90 and it is not known with certainty at which stage cyclisation occurs. Ring closure of 89 would lead to a tertiary centre at C_3 whereas protonation of 89 at C_3 would lead to the corresponding secondary intermediate which might be expected to give 90 on loosing nitrogen, and hence a primary carbanion in a possibly concerted process.

Treatment of the exomethylene ketone 80 with aluminium isopropoxide in isopropanol [113] effected a rearrangement rather than reduction and the product is thought to be a 1,3 hydroxy adamantyl ether (92. X = OiPr). Caglioti reduction also failed and this may be due to the facility with which the exomethylene and carbonyl groups interacted

in acidic media. The behaviour of the exomethylene ketone in acidic media was initially studied by UV, and it was noted that the addition of two drops of concentrated hydrochloric acid to an ethanolic solution of 80 caused a dramatic decrease im UV absorption (there was no absorption above 205 m).

Further investigation of this process in a variety of solvents was carried out however the products were complicated by the use of hydrochloric acid which produced the appropriate ether 92 accompanied by the chloro-alcohol 92 (X = Cl). Our investigations produced results in accord with those published by Stetter [114] at about this time and were not pursued further. From the products formed there is no evidence to support the intermediacy of 93, formed by protonation of the exomethylene group although Stetter has shown that 3,7-bis-exomethylene bicyclo(3,3,1)nonane (94) undergoes similar facile cyclisations (95).

Lithium aluminium hydride reduction of the exomethylene ketone 80 proceeded in a less stereospecific manner than that associated with the saturated ketones discussed in Section I, and provided the expected syn (endo) alcohol 97 (83%) and the anti (exo) epimer 96 (17%). These were readily separable by virtue of the non-polar properties of the hydrogen-bonded syn alcohol. GLC analysis of this compound even when pure displayed two peaks of R.I. 1195 and 1320. When the

sample was injected with the gas-flow off (preheater temperature 150°C) the relative intensity of the first peak was found to increase as the time interval before the resumption of gas-flow was increased, indicative of some thermal rearrangement. This aspect has not been fully investigated but the indications are that methyl oxyadamantane (R.I. 1195) is produced in a facile addition across the double bond of the suitably situated hydroxyl group. Both exomethylene alcohols (96 and 97) were stable at ambient temperatures.

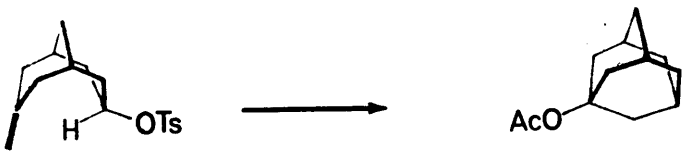
The NMR spectra of 96 and 97 have been discussed in Section I however the spectrum of 97 was of further interest, for in the absence of D_2O the hydroxyl signal was a <u>doublet</u> (J = 12 c/s) and the carbinyl signal was very broad (base width 30 c/s) and in the presence of D_2O the carbinyl signal was a much sharper multiplet (base width 18 c/s). This is interpreted as evidence of coupling between the carbinyl and hydroxyl protons with a coupling constant of 12 c/s, a large value for coupling of this type [115]. Such coupling has been observed in the system 98 [115] in which the dihedral angle through the C-O bond is 180° and if such an arrangement is a prerequisite for coupling of 12 c/s this implies that in 97 the hydroxyl proton, C_3 and carbinyl proton are coplanar as is the exomethylene group (assuming no lateral distortion in the bicyclo(3,3,1)nonane system) hence the hydrogen-bonding is in the manner shown in 97.

It had been decided to investigate the transannular participation, which throughout had plagued our investigations, by a study of the reactivities of the exomethylene tosylates 99 and 100. Following a standard procedure which proved adequate for the successful isolation of the reactive tosylates discussed in Section I, we were somewhat encouraged when initial attempts to prepare the anti tosylate (99) produced a tertiary alcohol identified as 1-adamantanol for this inferred that 99 was possessed of unusual reactivity. Modification of the work up procedure enabled the isolation and characterisation of the exomethylene tosylates, and it was shown that 1-adamantanol was produced when an ethereal solution of the anti tosylate was merely washed with dilute hydrochloric acid, whereas the syn tosylate 100 was isomerised to the trisubstituted olefinic tosylate 101 by similar treatment [112].

The NMR spectrum of the isomeric tosylate 101 is of interest insofar as the carbinyl signal is a multiplet at 5.10 (base width 18 c/s) and infers $J_{AX} + J_{BX} = 9$ c/s, which by the arguments detailed in Section I is evidence that the saturated ring is in a chair conformation. The carbinyl signal of the syn tosylate 100 was a multiplet at 5.30 (base width 18 c/s) with a sharp singlet for the exomethylene group superimposed at 5.24 (total integral 3H). Thus the ground state conformation of 100 is probably

TABLE 12.

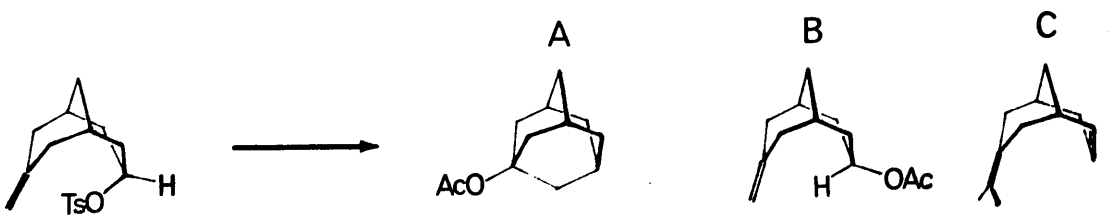
ACETOLYSIS PRODUCTS AND
KINETIC DATA.



99

$k = 6.56 \times 10^{-4}$ at 25°C $\quad \Delta H^{\ddagger} = 21.7$ Kcal./ Mole

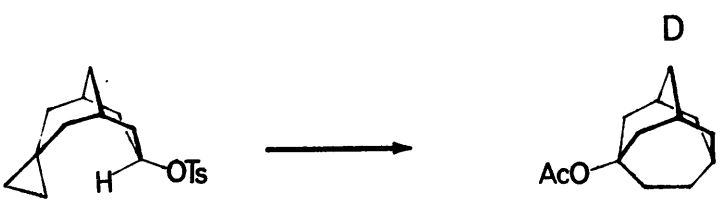
$k = 1.15 \times 10^{-2}$ at 50°C $\quad \Delta S^{\ddagger}_{25^\circ} = -1.5$ e.u.



100 82 3 15%

$k = 4.05 \times 10^{-5}$ at 25°C $\quad \Delta H^{\ddagger} = 21.7$ Kcal./ Mole

$k = 7.45 \times 10^{-4}$ at 50°C $\quad \Delta S^{\ddagger}_{25^\circ} = -5.6$ e.u.



114

$k = 2.14 \times 10^{-4}$ at 25°C $\quad \Delta H^{\ddagger} = 21.8$ Kcal./ Mole

$k = 3.98 \times 10^{-3}$ at 50°C $\quad \Delta S^{\ddagger}_{25^\circ} = -2.3$ e.u.

a distorted double chair as depicted.

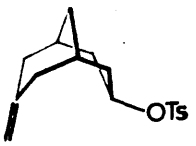
The exomethylene ketone 80 furnished the deuterated alcohols 102 and 103 on reduction with lithium aluminium deuteride, and the syn epimer 103 was separated and tosylated to furnish 105 in an attempt to prepare the deuterated ketone 104. Lithium aluminium reduction of the labelled syn tosylate (105) produced a mixture of the required exomethylene hydrocarbon (107, in very low yield) and predominantly dideuteroadamantane, presumably 106. The conversion of 107 to 104 was effected by ozonolysis, but this step also proceeded in low yield and the scheme was abandoned. Rearrangements in the course of hydride reductions have been observed in other investigations [116] nevertheless the extent of tricyclic product was somewhat surprising considering the stereochemistry of the starting material and compares with the behaviour of the syn tosylate (100) in acetolysis.

The syn- and anti-exomethylene tosylates (100 and 99) were solvolysed in anhydrous acetic acid buffered with sodium acetate, and rate measurements were carried out at 25° and 50°C (Appendix A). The anti tosylate gave a single product identified as 1-adamantyl acetate whereas the syn tosylate afforded a mixture of products (table 12).

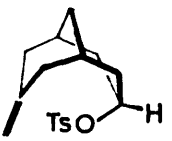
The acetates so produced were identified by comparison with authentic samples of 1-adamantyl acetate (A) and anti-exomethylene acetate (B), and the olefin was isolated and

TABLE 13.

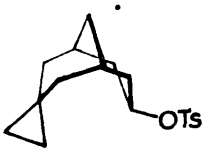
RELATIVE SOLVOLYTIC REACTIVITY AT 25°C.



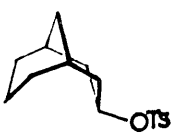
13500



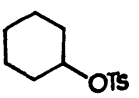
850



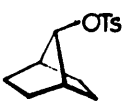
4375



1200

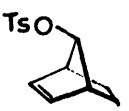


1



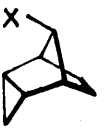
10^{-7}

7600



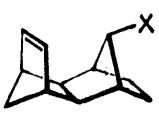
10^{-3}

10^{7}

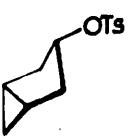


5×10^{-7}

3×10^{-8}



2000



15

Data from ref. 69, 91, 99, 118, 119.

shown to be homogeneous to GLC. The NMR spectrum of the olefinic product in pentane afforded sufficient information to identify the product; a complex AB signal at 4.45, 4.50 and 4.60 (2H olefinic) and a split exomethylene signal at 5.40 and 5.50 compatible with the non-equivalent exomethylene protons present in 7-exomethylenebicyclo(3,3,1)-non-2-ene (C).

The rate of reaction of the anti tosylate (99) indicates clearly that anchimeric assistance occurs in the solvolysis for as noted in Section I, the introduction of a trigonal centre at C_3 or C_7 results in a considerable decrease in the I-strain of the system, thus the unassisted rate of solvolysis of 99 might be expected to compare with that of cyclohexyl tosylate, rather than that of 3-exobicyclo(3,3,1)nonanyl tosylate (table 13). A measure of the anchimeric assistance may be obtained from Schleyer's equation (Section I, p 30). Since the stretching frequency of the carbonyl of the exomethylene ketone is 1717 cm^{-1} the calculated unassisted rate (relative to cyclohexyl tosylate at 25°C) is 0.56, assuming that torsional and nonbonded interaction strains are negligible, thus there is anchimeric assistance of the order of $10^{4.4}$.

The anchimeric assistance in ionisation of the anti tosylate (99) may be represented by 108, however there is little evidence that the product forming intermediate is

other than the classical 1-adamantyl carbonium ion. The rate of acetolysis of 1-adamantyl tosylate has been determined by Schleyer, $k = 5.86 \times 10^{-4}$ sec^{-1} at 25.0°C [104], and is comparable with that of the anti exomethylene tosylate (table 12). In view of the similarity in rates of these two compounds (within 11%) measured using different methods, the intermediacy of 1-adamantyl tosylate in the course of solvolysis of the anti exomethylene compound could not be discounted. If the ionisation of the exomethylene tosylate and subsequent collapse of the intimate ion pair to 1-adamantyl tosylate were more rapid than the latter then the overall kinetics of the process would reflect the ionisation of 1-adamantyl tosylate.

To check whether such a process was occurring in the solvolysis of the anti exomethylene tosylate required either an independent rate measurement based on some time dependent variable other than the formation of tosylate anion, or the isolation and identification of the reaction intermediates. In the particular case above it might be possible to follow the rate of ionisation of the anti exomethylene tosylate directly by monitoring the NMR signal of the exomethylene group in the course of solvolysis, however the occurrence of 1-adamantyl tosylate could be detected in the presence of anti exomethylene tosylate readily by NMR spectroscopy and this seemed the more expedient solution.

A sample of the crystalline anti exomethylene tosylate was dissolved in buffered acetic acid and allowed to react for 8 minutes at room temperature to approximately 27% completion ($t_{\frac{1}{2}}$ = 17 minutes at 25°C) then the reaction was worked up carefully to afford an oil containing unreacted tosylate(s) and 1-adamantyl acetate, which was examined by NMR (see figure 9). Both anti exomethylene and 1-adamantyl tosylates would produce signals at A, B and E (a symmetrical A_2B_2 system, distorted by traces of $CHCl_3$, and an aromatic methyl resonance) but only the anti exomethylene tosylate would produce the signals observed at C and D (nine line carbinyl signal and an exomethylene singlet). The production of 1-adamantyl acetate can be detected in the peak F (acetate methyl group) and obviously does not affect the peaks A-E. In the absence of 1-adamantyl tosylate the relative integration of A:B:C:D:E should be 2:2:1:2:3 whereas the presence of 1-adamantyl tosylate should be marked by a relative increase in the ratios of A, B and E to C and D. Three integration curves were obtained and if the values for B (the distorted half of the A_2B_2 signal) are discounted the results can be seen to be consistent with the presence of 93 - 98.5% anti exomethylene tosylate. Thus within the limits of experimental error there is no evidence to support the intermediacy of 1-adamantyl tosylate. The independent rate measurements are in this sense vindicated and may reflect slightly

different ground state energies of the two compounds.

In the systems 23, 26 and 40 discussed in the introduction, there is significant ion pair return affording rearranged derivatives which were successfully isolated due to their comparatively unreactive nature [85 91]. It is noteworthy that the bridged ion 41 gives both acetate and brosylate of rearranged structure (42, X = OAc, OBs) whereas the intermediate ion pair in the solvolysis of the anti exomethylene tosylate does not apparently afford isomeric tosylate. This may be a result of the distance apart of the cationic centre from the site of ionisation, in the respective intermediates 41 and 109.

There is evidence from the products of solvolysis of the syn exomethylene tosylate (100) of two product forming intermediates: unassisted ionisation would produce the cation 110 which by analogy with the simple 3-cation (Section I) would furnish predominately olefin C, and acetate B (table 12). The subsequent participation of the double bond could explain the absence of syn exomethylene acetate, the 3-endo epimer of B, and the main solvolysis product A, via the classical tertiary 1-adamantyl cation (109) which from the product distribution is appreciably more stable than the secondary cation 110.

That the rate determining step in the solvolysis of the syn tosylate is not effectively assisted by the exomethylene group can also be seen from the relative

rate data in table 13. Although the introduction of an exomethylene group at C_7 considerably lessens the I-strain of such systems as 99 and 100 relative to the C_7 saturated compounds (Section I), the ground state energy of the syn tosylate may be appreciably higher than that of the anti epimer due to the increased steric congestion associated with a C_3 endo substituent in the bicyclo(3,3,1)nonane system. Thus steric acceleration due to the relief of I-strain is to be expected in the solvolysis of the syn tosylate, whatever the preferred ground state conformation. If the conformation of the syn tosylate is a distorted double chair (100) the possibility exists of steric acceleration in ionisation resulting from the relief of nonbonded interaction strain [50] associated with the decrease in crowding of the transition state (111). These two effects may adequately account for the observed relative reactivity, 850 times that of cyclohexyl tosylate at 25°C.

We were interested in prep ring the corresponding cyclopropyl alcohols 112 and 113, and converted the anti exomethylene alcohol (96) into anti-7-spirocyclopropyl-bicyclo(3,3,1)nonan-3-ol (112) in a Simmons-Smith reaction.[117] It is of interest that this reaction failed to proceed to completion even after an extended reaction period and this may reflect the difficulties involved in converting a

trigonal C_3 (or C_7) atom into a tetrahedral product as discussed in Section I. The syn cyclopropyl alcohol (113) has not yet been prepared, for under the same conditions the syn exomethylene alcohol (97) was rapidly converted to the cyclic ether 114, which could be readily prepared by acid-catalysed isomerisation of the syn alcohol (97). Alternative synthetic routes to 113 have not as yet been studied, but a comparison of the properties of the syn exomethylene and cyclopropyl alcohols and the corresponding ketones (80 and 120) will be of interest.

The anti cyclopropyl tosylate (115) was prepared and, on solvolysis in buffered acetic acid, produced a single product (table 12) identified as 3-homoadamantyl acetate (D) by reduction to the alcohol and comparison with an authentic sample of 3-homoadamantanol (118), kindly supplied by Professor P. von R. Schleyer. The mass spectra of the two alcohols were identical and could be readily distinguished from those of the isomeric alcohols 112 and 119. The product of solvolysis is thus consistent with cyclopropyl participation and the rate of reaction would lead us to conclude that this is involved in anchimeric assistance. A more precise estimate of this is precluded by the lack of information e.g. the carbonyl stretching frequency of the parent ketone 120 which is not as yet to hand.

An examination of models suggests that there is considerably greater transannular crowding in the anti cyclopropyl tosylate (115) than in the anti exomethylene derivative (99) and that this may be relieved after ionisation. If cyclopropyl participation, i.e. ring opening and relief of the inherhent I-strain therein, is synchronous with ionisation it might be expected that the cyclopropyl derivative would be more reactive. This is not the case, the anti cyclopropyl tosylate is found to be 3 times less reactive than the exomethylene compound and this must surely reflect on the relative stabilities of reaction intermediates. If the classical cations 117 and 109 respectively are involved, this implies a lower total energy content is associated with the 1-adamantyl cation than the 3-homoadamantyl cation as has been suggested previously,[106] but it leaves open the question of the possibly unique stabilisation of the 1-adamantyl cation.

Recently Schleyer has shown in a computer analysis of bridgehead reactivity that 1-adamantyl derivatives are some 400 times more reactive than would be expected from basic calculations which afford results in excellent agreement with other bridgehead derivatives and although these preliminary data may yet be refined the possibility of some special feature stabilising the 1-adamantyl carbonium ion

remains. Thus our finding of greater reactivity associated with double bond participation than cyclopropyl, may be a special case rather than an example of a general trend.

The recent investigations in the solvolysis of endo-anti-bicyclo(3,2,1,0 ^{2,4})octan-8-yl p-nitrobenzoate (121) have shown that the compound is exceedingly reactive compared with the 7-norbornyl system (10^{14}) and related isomeric and epimeric compounds (table 13) [118 119]. As predicted by Hofmann [103] in general terms the cyclopropyl derivative (121) was found to be more reactive than the corresponding 7-norbornenyl compound by a factor of 10^3 at 100°C. Such a large increase in reactivity may not be general, however, for the cyclopropyl compound 121 may be more reactive due in part to the relief of I-strain not present in the olefinic case. Certain geometric factors in the cyclopropyl compound 121 favour the formation of a uniquely stable tris-homocyclopropenyl cation 122 compared with the cis-bicyclo(5,1,0)hexyl system (58) for the puckered 5 membered ring present in the former results in a closer proximity of the potential cationic centre with the cyclopropyl ring [119], and this may be the most important factor contributing to the large difference in reactivity between the two systems. The products of solvolysis of 121 are consistent with the intervention of

the tris-homocyclopropenyl cation 122, scheme 3.

As yet it is not possible to compare with accuracy the relative efficiency of double bond and cyclopropyl participation. One simplification of the problem however, is the possible formation of the same intermediate carbonium ion by both double bond and cyclopropyl participation. Such systems as 123 and 125 may ionise with assistance from the exomethylene groups to give the 3-homoadamantyl cation and comparison with the cyclopropyl derivative 115 would be of interest. The involvement of dissimilar non-classical intermediates 124, 126 and 116 rather than the common classical intermediate 117, might be detectable for in the solvolysis of 1-adamantyl methyl tosylate (127) the non-classical intermediate 126 has been suggested to account for the formation of mainly 3-homoadamantyl acetate (93.2%) accompanied by 1-adamantyl methyl acetate in buffered acetic acid [120]. Thus bridged ring systems may prove to be invaluable in providing a fuller understanding of the nature of chemical reactions.

The comments preceeding the first experimental section are relevant and in addition melting points in this section denoted "s.c." were measured in sealed capillaries using a Gallenkamp melting point apparatus.

Tetrahydrodicyclopentadiene.

Technical grade dicyclopentadiene (3.5 Kg) was purified by distillation under reduced pressure to give a low melting solid (b.p. 66-67° @ 16mm, n_D^{22} = 1.5123, literature value n_D^{22} = 1.5120) which was hydrogenated in 1 Kg batches. Dicyclopentadiene (1Kg), ether (200 mls) and platinum oxide (5g) were placed in a high pressure hydrogenation apparatus and subjected to hydrogenation at 50 atmospheres pressure for 10 hours. The initial uptake of hydrogen was rapid and a temperature rise of 60°C was noted. The catalyst was removed by suction filtration over Celite 535, and the ether was distilled under reduced pressure. Unreacted starting material (50-100 g) was then distilled from the product which on cooling afforded a wax-like solid (90-95%) of m.p. 65-67°C.[121]

Adamantane.

This hydrocarbon (350 g) was prepared from tetrahydrodicyclopentadiene (2.80 Kg) by treatment with $AlCl_3$ at 160°C[121]. Recrystallisation from light petroleum at -70°C, followed by sublimation under reduced pressure afforded colourless crystals of m.p. 268-269° s.c., in agreement with the literature as was the infra-red [122] and mass spectra [123].

1-Bromoadamantane.

Bromination of adamantane (60 g) according to the method of Stetter [124] resulted in 1-bromoadamantane (70 g) which was purified by low temperature recrystallisation from methanol followed by sublimation to give colourless crystals, m.p. 117-118°C (literature 118° [124]), ν_{max} (mull) 2900, 2700, 1290, 1100, 1025, 950, 812, 770 and 680 cm^{-1}.

1-Adamantanol.

1-Adamantanol (2.50 g) was prepared from 1-bromoadamantane (5.0 g) following the method of Stetter [124]. Recrystallisation from aqueous tetrahydrofuran, followed by sublimation gave colourless crystals, m.p. 276-278°C s.c. (literature 282°C [124]), ν_{max} (CCl_4, high resolution) 3606, 2931, 2912, 2849, 1458, 1358, 1333, 1308, 1120, 1106, 1092, 979 and 929 cm^{-1}. Mass spectral parent ion, 152.

1-Adamantanecarboxylic acid.

(a) The carboxylic acid (150 g) was prepared from adamantane (165 g) by the method of Koch and Haaf.[125 126] Three recrystallisations from aqueous methanol afforded crystals of constant m.p. 174-177°C (literature 174-177°C [125], 181°C [127]).

(b) Carboxylation of 1-bromoadamantane (60 g) by the method of Stetter and Rauscher [127] resulted in 1-adamantanecarboxylic acid (40 g) of m.p. 177-179°C, after recrystallisation from aqueous methanol.

1-Adamantyl methyl carbinol (119)

1-Adamantanecarboxylic acid (0.100 g) was esterified with excess diazomethane and the ester treated with lithium aluminium hydride to afford the alcohol (119) as a crystalline solid after normal isolation procedure, ν_{max} (mull) 3350, 2650, 1340, 1150 and 1060. The Mass spectrum was in agreement with published data,[123] parent ion, 166.

3-Bromoadamantane-1-carboxylic acid (128)

The apparatus used for the bromination of 1-adamantanecarboxylic acid is described by Stetter and Wulff.[128] A simplified piece of equipment was constructed in these laboratories and used according to the method of Stetter and Meyer [109].

Dry bromine (100 ml, distilled from P_2O_5) and anhydrous aluminium bromide (60 g) were added to a conical flask, with a glass covered bar-magnet, under an atmosphere of dry nitrogen. Adamantanecarboxylic acid (30 g) was placed in a container (which permits slow addition in a closed system) and this, surmounted by a reflux condenser, was placed on top of the conical flask which was immersed in a cooling bath ($CCl_4/CO_{2(s)}$) maintained between -5° and $0^\circ C$. The carboxylic acid was added portionwise to the stirred bromine solution over a period of 4 hours, then the reaction was maintained between 0° and $10^\circ C$ for 48 hours, and finally kept at room temperature for 10 hours. The contents of the reaction flask were then poured onto crushed ice (500 g), and chloroform (300 ml) was added. The excess bromine was destroyed by treatment with solid sodium metabisulphite (with stirring) and the organic phase was then separated and the aqueous phase extracted with chloroform (2 x 50 mls). The combined chloroform extracts were washed with water (3 x 250 ml), N sodium hydroxide solution

(1 x 250 ml) and finally with 0.5 N sodium hydroxide solution (2 x 100 ml). The combined alkaline extracts were washed with ether (1 x 100 ml), then acidified with dilute sulphuric acid (2N) and the resultant precipitated acid allowed to stand overnight, filtered then dried.

Whereas Stetter [109] reports a 68% yield (29.3 g) of 3-bromoadamantane-1-carboxylic acid of m.p. 146.5°C s.c., after recrystallisation from cyclohexane, our experiments were less successful. Of the eleven runs attempted in these laboratories, six were unsuccessful and afforded only starting material. The eighth run in which a two fold excess of aluminium bromide was used afforded a mixture of carboxylic acids of m.p. 162-163°C which could not be fractionally crystallised. Analysis indicated that a considerable quantity of dibromo-acid was present. Found C 42.15, H 4.62; $C_{11}H_{15}BrO_2$ requires, C 50.75, H 5.75; $C_{11}H_{14}Br_2O_2$ requires C 38.8, H 4.10%. The product of further bromination is considered to be 3,5 dibromoadamantane-1-carboxylic acid (131) although this product was not further characterised. Of the four successful runs, the yields varied from 15 to 55% of mono-bromo-acid (128) m.p. 144-146°C s.c., ν_{max} (mull) 3000 (broad), 2900, 2650, 1700, 1290, 1265, 1240, 980, 905, 835 and 700 cm^{-1}.

The monobromo-acid (128) was then converted in high yield into 3-bromoadamantane-1-carboxylic amide (129) by

standard procedures and recrystallised from benzene in plates, m.p. 154-155°C (literature 154-155°C [110]).

N-(3-Bromoadamantyl-1)-methylurethane (130)

A solution of sodium (1.0 g) in dry methanol (25 ml) was reacted with a solution of 3-bromoadamantane-1-carboxylic amide (4.75 g) in dry methanol (25 ml). Dry bromine (1 ml) was then dropped into the stirred, ice-cold solution, the reaction flask slowly warmed to 55°C and the contents of the flask then poured into cold water (200 ml). The crystals so produced were filtered off, dried and recrystallised from light petrol, to give the required methyl urethane (130) in 95% yield (5.05 g). m.p. 82-83°C (literature, 82.5-83.5°C [110]).

7-Exomethylenebicyclo(3.3.1)nonan-3-one (80)

The bromo urethane (130, 40 g) was added to a dilute solution of sodium hydroxide (10%, 400 mls) and the mixture heated under reflux. After approximately 90 minutes the product volatilised from the solution and was washed from the reflux condenser with ether from time to time thereafter, and the reaction was complete in 4-6 hours. The ether washings were dried ($MgSO_4$) and the solvent evaporated slowly. Recrystallisation from light petrol afforded the exomethylene ketone (80) as colourless crystals (17.0 g 81 %) of m.p. 162-163°C s.c. (literature, 162-163°C s.c. [110]), ν_{max} (CCl_4, high resolution) 3069, 2977, 2918, 2886, 2846, 2828, 2798, 1717, 1699(w), 1652, 1443, 1406, 1341, 1333, 1224, 1096, 1066, 906 and 894 cm^{-1}. Mass spectral parent ion, 150. NMR (60 Mc) singlet @ 5.20 (2H), broad peak @ 7.60 (10H) and a broadened singlet @ 8.05 (2H).

(i). Lithium Aluminium Hydride Reduction

A solution of the exomethylene ketone 80 (1.218 g 8.12 mM) in dry ether (50 ml) was added dropwise to a stirred slurry of lithium aluminium hydride (0.31 g 8.17 mM) in ether (25 ml) at room temperature over 30 minutes, and thereafter the solution was heated under reflux for 2 hours. The excess hydride was then destroyed by the careful dropwise addition of saturated sodium sulphate solution till th cloudy ether solution cleared and the insoluble inorganic salts settled. The ether solution was decanted from the inorganic material which was then dissolved in water (50 ml), and extracted with ether (3 x 50 ml). The combined ether solutions were then washed once with dilute sulphuric acid (0.06 N, 25 ml) saturated sodium bicarbonate solution, brine, and dried (Na_2SO_4). Removal of the solvent under reduced pressure at room temperature afforded a white finely crystalline solid (1.200 g, 97%). TLC showed the product to be a mixture of two compounds with a marked predominance of one (r_f 0.60) over the other (r_f 0.45). GLC analysis of the products showed two peaks (see text). Separation of the products was readily effected by preparative TLC or by chromatography and gave the less polar compound (0.993 g)

as fine white needles of m.p. 49-50°C and the slower-running product (0.152g) as needles of m.p. 89-90°C

The lower melting epimer was considered to be syn-7-exomethylenebicyclo(3,3,1)nonan-3-ol (97) in view of the occurrence of intramolecular hydrogen bonding, unchanged on dilution. Found; C 78.65, H 10.80, $C_{10}H_{16}O$ requires; C 78.90. H 10.60%. ν_{max} (CCl_4, high resolution) 3516, 3071, 1643, 1462, 1444, 1117, 1090, 1060, 1004, 992, 962, 905, and 888 cm^{-1}. The mass spectrum was significantly different from its epimer, parent ion 152. NMR (60 Mc) in $CDCl_3$, a singlet @ 5.08 (2H, exomethylene group deshielded relative to epimer), a broad multiplet @ 6.25 (carbinyl H, base width 30 c/s; 18 c/s in the presence of D_2O), a doublet @ 6.95 and 7.15 (1H, hydroxylic proton absent in the presence of D_2O), singlet @ 7.70 (4H) superimposed on complex methylene resonance @ 7.85, 8.15 and 8.40 (8H).

The higher melting epimer, anti-7-exomethylene-bicyclo(3,3,1)nonan-3-ol (96) found; C 78.40, H 10.35: $C_{10}H_{16}O$ requires; C 78.90 H 10.60%. ν_{max} (CCl_4, high resolution) 3624, 3071, 1663, 1645, 1467, 1448, 1175, 1114, 1088, 1049, 967, 930 and 891 cm^{-1}. The mass spectrum was identical with that of 1-adamantanol, parent ion 152. NMR (60 Mc) in $CDCl_3$, a singlet @ 5.36 (2H, exomethylene group), overlapping a septet centred @ 5.50 (1H, carbinyl, J_{AX} = 11.0, J_{BX} = 5.5 c/s), a singlet @ 7.70 (4H)

superimposed on complex methylene resonance @ 7.85, 8.02, 8.12, 8.42 (8H).

NMR data was also obtained in CCl_4 solution (100 Mc).

(ii) Lithium Aluminium Deuteride Reduction

Reduction of the exomethylene ketone (80) with an equimolar amount of this reagent gave the expected mixture of monodeuterated alcohols (102 and 103) with the same syn : anti ratio of 5 : 1. Separation of the epimers was equally facile, and afforded each epimer as a pure crystalline solid.

Syn epimer (103), m.p. 49-50°C, ν_{max} (CCl_4, high resolution) 3516 (unchanged with dilution), 3071, 2165, 1644, 1635, 1462, 1129, 1090, 949, 903 and 884 cm^{-1}. Mass spectrum indicated at least 95% deuterium incorporation, parent ion 153. NMR (60 Mc) in $CDCl_3$, indicated the absence of carbinyl proton resonance, singlet @ 5.08 (2H), singlet @ 7.05 . (1H, hydroxyl) singlet @ 7.70 (4H), and singlet 7.88 (2H), doublet @ 8.10 and 8.20 (2H) and a complex signal @ 8.40 (4H).

Anti epimer (102), m.p. 92-93°C, ν_{max} (CCl_4, high resolution) 3623, 3070, 2917, 1643, 1465, 1110, 1094, 1075, 950 and 889 cm^{-1}. Mass spectrum indicated at least 95% deuterium incorporation, parent ion 153. NMR (60 Mc) in

in $CDCl_3$, indicated the absence of carbinyl proton resonance, singlet @ 5.36 (2H), singlet @ 7.70 (4H), singlet @ 7.90 (2H) singlet @ 8.10 (2H) and a complex signal @ 8.42 and 8.68 (5H, integrating for 4H after D_2O exchange).

(iii) Sodium Moist Ether Reduction

Sodium (75 mg) was added in finely cut pieces to a stirred solution of the exomethylene ketone (80, 0.230 g), water (0.1 ml) and ether (20 ml) maintained at 0°C. When the sodium was consumed, fresh peices (75 mg) were added followed by water (0.1 ml) and this sequence was repeated for 12 hours then excess water (20 ml) was added. The ether layer was separated and the basic aqueous layer extracted with ether (2 x 10 ml). The combined ether solutions were then washed with brine and dried (Na_2SO_4). TLC showed one main spot (rf 0.45) and a trace of starting material (rf 0.50). Removal of the solvent afforded a white solid $_{OH}$ 3490 with no olefinic absorption. Successive recrystallisations from light petrol removed the ketonic impurity and gave a white crystallisatine product (0.18 g) of m.p. 165-166°C. Found; C 78.70, H 10.75 $C_{10}H_{16}O$ requires; C 78.90, H 10.60%. $_{max}$ (mull) 3400, 1475, 1320, 1230, 1150, and 1042 cm^{-1}. NMR (60 Mc) in $CDCl_3$, a broad unresolved resonance @ 7.80 (2H), singlet @ 8.15 (4H), singlet @ 8.38 with overlapping complex @ 8.50 (6H), sharp singlet superimposed @ 8.40 (hydroxyl proton) and sharp singlet @ 9.00 (3H, methyl group). Mass spectral parent ion 152. The product was assigned the structure, 7-methyltricyclo(3,3,1,$0^{3,7}$)nonan-3-ol (85).

Attempts to prepare the corresponding toluene-p-sulphonate ester, under standard conditions resulted in unreacted starting material (85).

(iv) Attempted Meerwein-Pondorff-Verley Reduction [113]

A solution of the exomethylene ketone (0.50 g, 3.35 mM) and freshly prepared [129] aluminium isopropoxide (2.04 g 10 mM) in dry isopropanol (50 ml) was slowly distilled with concomitant addition of dry isopropanol to maintain the volume of solvent over a period of 5 hours. The distillate failed to form a 2:4 dinitrophenylhydrazone derivative during the entire reaction period, suggesting that no reduction had occurred. However, the reaction mixture was cooled, diluted with brine, then extracted three times with ether. The combined organic extracts were then washed once with brine and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure afforded a colourless gum, containing some unreacted ketone plus a hydroxylic product, ν_{max} (film) 3400, 2650, 1390, 1375, 1350, 1310, 1220, 1130, 1100, 1070, 1050, 1030, 980, 960, 940, 850 and 760 cm^{-1}. TLC showed that the product was not compatible with the epimeric alcohols 96 and 97 and GLC analysis indicated the presence of three products of retention times 12.8 min. (10%), 17,7 min. (80%) and 21.2 min. (10%) using a 10% Polyethylene Glycol Adipate Column at 150°C. There is evidence that the main product may be the cyclised ether 92 (X = OiPr) but the reaction has not been further investigated.

(v) Attempted Caglioti Reduction [130]

A solution of the exomethylene ketone (0.40 g 2.7 mM) and toluene-p-sulphonylhydrazine (0.56 g 3.0 mM) in absolute ethanol (15 ml) was heated under reflux for 15 minutes. The solution w s cooled, then reduced in volume, but all attempts to induce crystallisation failed. Complete removal of the solvent afforded an oily gum with no carbonyl nor exomethylene absorption suggesting that cyclisation occurred rather than the formation of the required tosyl hydrozone derivative 134. The structure of this initial product has not been established and possible compounds are 132 and 133, neither of which would be expected to undergo reduction with sodium borohydride. In the event when the initial product (70 mg) was treated with sodium borohydride (250 mg) in dioxane (10 ml) under reflux for 1 hour, normal isolation procedure failed to give any hydrocarbon products. This method of reduction was not studied further, nor were the products further characterised.

(vi) Modified Wolff-Kishner Reduction

Sodium (0.10 g 4.3 mM) was dissolved in diethylene glycol (16 ml), exomethylene ketone (0.20 g 1.3 mM) was added followed by 100% hydrazine hydrate (1.0 ml) and the reaction was heated under reflux, as described in section J. The product was isolated as a colourless oil and was adsorbed on alumina. Elution with pentane afforded a colourless crystalline compound (0.05 g 30%) homogeneous to TLC and to GLC analysis. Comparison on a 20% tris-cyanoethoxypropane column at 50°C showed that the product (retention time 3.3 min.) was incompatible with 3-exomethylenebicyclo(3,3,1)nonane (10 min.) and adamantane (9.12 min.). The product ν_{max} (CCl_4 solution) 2970, 1455, 1375, 1325, 1298, 1130, 1100 and 1080 cm^{-1}. NMR (100 Mc), broad singlet @ 7.82 (2H), complex signal @ 8.18 to 8.70 (5H) overlapping singlet @ 8.45 (6H), and a very sharp methyl singlet @ 8.85 (3H), was assigned the structure 3-methyl tricyclo($3.3.1.0^{3,7}$)nonane (88)

Acid Catalysed Cyclisation of
7-Exomethylenebicyclo(3.3.1)nonan-3-one

(a) The exomethylene ketone (92 mg) was added to dilute sulphuric acid (6N. 5 ml) and sufficient tetrahydrofuran was added to obtain a homogeneous solution which was warmed on a steam-bath for 10 minutes and then allowed to cool. The solution was diluted with brine, extracted thoroughly with ether, then the ether extracts were combined, washed with brine, then dried (Na_2SO_4). Removal of the solvent under reduced pressure furnished a colourless crystalline product (80 mg) of m.p. 175-175.5°C, ν_{max} (mull) 3350, 2700, 1380, 1370, 1350, 1330, 1300, 1235, 1200, 1135, 1100, 1030, 950 and 910 cm^{-1}. Mass spectral parent ion, 168. The product was assigned the structure of adamantane-1,3-diol (92, X = OH).

The mass spectrum of this compound was almost identical with that of the exomethylene ketone (80).

(b) The exomethylene ketone (85 mg) was warmed in isopropanol, to which concentrated sulphuric acid (3 drops) had been added. Work up as above gave an oily gum which was compared with the anomolous product from Meerwein Pondorff Verley reduction of the same ketone (80); ν_{max} (film) 3400, 2650, 1390, 1375, 1350, 1310, 1220, 1130, 1110, 1050, 980, 960, 940, 850 and 830 cm^{-1}. The infra-red spectra and GLC were compatible (one product being obtained in this reaction).

Cyclisations in other solvents were also carried out, catalysed by sulphuric and hydrochloric acids, however a more detailed account of these products may be obtained in Stetter's publication, [114] which appeared at the time of these experiments.

3-Exomethylenebicyclo(3.3.1)nonane

A solution of syn-7-exomethylenebicyclo(3,3,1)nonan-3-yl toluene-p-sulphonate 100 (0.140 g 0.46 mM) in ether (20 ml) was added to s slurry of lithium aliminium hydride (0.150 g 3.95 mM) in ether (10 ml) and the reaction heated under reflux for 90 minutes. Normal isolation procedure and careful removal of the solvent under reduced pressure at room temperature produced a pale green oil, which solidified below 0°C ν_{max} (film) 3010, 2970, 2700, 1650s, 1380, 1340, 900s, 810 and 720 cm^{-1}. (consistent with a mixture of adamantane and 3-exomethylenebicyclo(3,3,1)-nonane) and 1360, 1190 and 1130 cm^{-1}. (impurities, possibly sulphonic ester by-products). The material was adsorbed on alumina and elution with light petroleum afforded the hydrocarbon products as a colourless semi-solid (50 mg 75%) which was shown to be a 4:1 mixture of adamantane and exomethylene hydrocarbon by GLC analysis. The two hydrocarbons were not separated.

This reaction was not investigated further, except to establish the stability of the exomethylene hydrocarbon to hydride, as follows; a pure sample of the exomethylene hydrocarbon [131] was subjected to lithium aluminium deuteride in ether, and the reaction heated under reflux for 14 hours, and the exomethylene hydrocarbon isolated without change.

(D) A solution of the above mixture of adamantane and 3-exomethylenebicyclo(3,3,1)nonane (0.20 g) in ethyl acetate (30 ml) was cooled to -70°C in an acetone-$CO_{2(s)}$ bath and a stream of ozone gently bubbled through the solution for some hours until a blue colouration persisted. The reaction was allowed to warm slowly to room temperature then glacial acetic (10 ml) and zinc dust (0.15 g) were added and the solution stirred overnight at room temperature to decompose the ozonide. The reaction mixture was filtered free from insoluble material which was washed thoroughly with light petrol. The ethyl acetate solution was diluted with brine and extracted with light petrol (3 x 20 mls). The combined petrol solutions were washed once with saturated sodium carbonate solution followed by brine then dried ($MgSO_4$). Removal of the solvent produced a colourless crystalline solid. TLC indicated the presence of three compounds, a hydrocarbon (rf 1.00), ketonic product (rf 0.50) and a trace of a more polar material (rf 0.30). Preparative TLC effected a separation of the hydrocarbon (the infra-red spectrum was superposable on that of adamantane) and the ketone (15 mg ca. 35%) ν_{max} (mull) 1710, 1420, 1380, 1360, 1350, 1240, 1235, 1140, 1120, 1100, 960, 930, 890, 870, 820 and 780 cm^{-1} superposable on an infra-red spectrum of an authentic sample of 3-bicyclo(3,3,1)nonanone. The GLC behaviour of the two ketones was also identical.

7,7-Dideuterobicyclo(3.3.1)nonan-3-one (104)

The monodeuterated syn alcohol (103) resulting from lithium aluminium deuteride reduction of the exomethylene ketone (80) was purified and the toluene-p-sulphonate ester (105) prepared as before. The tosylate (1.10 g 3.58 mM) was dissolved in ether (50 ml) and added to a solution of lithium aluminium deuteride (0.60 g 14.3 mM) in ether (50 ml). The reaction was heated under reflux for 90 minutes and the products isolated as before as an oily solid, ν_{max} (film) 3010, 2970, 2700, 2200, 1650, 1460, 1350, 900s and 700 cm^{-1}.

The mixture of deuterated adamantane (106) and 7,7-dideutero-3-exomethylenebicyclo(3,3,1)nonane (107) was not separated but was subjected to a modified ozonolysis procedure using tetracyanoethylene [132]. The yield of ketone produced was exceedingly low and after chromatographic separation a colourless crystalline product (10 mg) was isolated ν_{max} (mull) 2970, 2230, 2150, 1710, 1470, 1450, 1420, 1375, 1355, 1330, 1235, 1175, 1110, 1080, 1010, and 740 cm^{-1}. and has been assigned the structure 7,7-dideuterobicyclo(3.3.1)nonan-3-one (104) although this product has not been fully characterised. The hydrocarbon also obtained on chromatography was a highly crystalline product ν_{max} (mull) 2970, 2650, 2180, 1460, 1390, 1350, 1105, 1030, 1000, 980, 790 and 765 cm^{-1}. and was assigned

the structure 1,3-dideuteroadamantane (106). The mass spectral parent ion, 138 was the base peak.

Anti-7-exomethylenebicyclo(3.3.1)nonan-3-yl Toleune-p-sulphonate (99)

A. Initial attempt.

The anti exomethylene alcohol (96, 0.020 g) was treated with toluene-p-sulphonyl chloride (0.033g 1.3 Mxs) in the usual manner (in which in the course of work up the ether extracts are washed thoroughly with 6N hydrochloric acid) and afforded a colourless solid, ν_{OH} 3350 cm^{-1}. The product was shown by TLC to be a mixture of two compounds (rf 0.3 and 0.7) which were readily separated by preparative TLC.

The less polar material (5 mg) was identified as toluene-p-sulphonyl chloride by its infra-red spectrum, whereas the crystalline alcohol (10 mg) ν_{max} (mull) 3350, 1170, 1115, 1100, 1085, 985, 935 and 820 cm^{-1}. was incompatible with the starting alcohol whereas the TLC and GLC behaviour was identical with 1-adamantanol.

B. Modified Procedure.

The anti exomethylene alcohol (96, 0.030 g) was treated with toluene-p-sulphonyl chloride (0.042 g, 1.1 Mxs) in pyridine at 0°C over night, then poured onto water (30 ml), and extracted with pentane (3 x 20 mls). The combined organic phase was washed repeatedly with cold water (6 x 20 mls) to remove pyridine, then saturated sodium bicarbonate solution (1 x 30 ml) and brine (1 x 30 ml) then dried ($MgSO_4$).

Removal of the solvent without heating provided anti-7-exo-methylenebicyclo(3.3.1)nonan-3-yl toluene-p-sulphonate (99) as a crystalline solid (0.05 g) which was recrystallised from pentane to furnish small prisms of m.p. 75-76°C; ν_{max} (mull) 1650, 1180, 1100, 930, 880, 860, 820, 790, 720 and 660 cm^{-1}. Found; C 66.60, H 7.25 $C_{17}H_{22}SO_3$ requires; C 66.65, H 7.25%. NMR (60 Mc), A_2B_2 quartet @ 2.16-2.75 (4H, aromatic ring) a nine line multiplet centred @ 4.60 (1H, carbinyl; X part of an A_2B_2X system J_{AX} = 11.0, J_{BX} = 6.0 c/s), sharp singlet @5.30 (2H, exomethylene), sharp singlet @ 7.56 (3H, aromatic methyl group) and 4 groups of peaks @ 7.70-8.80 (12H).

C. Effect of dilute mineral acid.

(i) A sample of anti exomethylene tosylate (99, 0.060 g) was dissolved in ether (50 ml) in a 100 ml flask, and dilute sulphuric acid (6N, 30 ml) was added. The stoppered flask was shaken for 3 hours at room temperature then the organic layer was separated, washed with satur ted sodium bicarbonate solution, brine, then dried (Na_2SO_4). Removal of the solvent afforded a semi-solid (0.025 g); ν_{max} (film) 3350, 1600, 1190, 1180, 1115, 1100, 1035, 1000, 930 and 660 cm^{-1}. TLC indicated that the main product (rf 0.3) was accompanied by traces of 3 less polar compounds (rf 0.7-0.85). A sample (5 mg) of this crude product was dissolved in ether and shaken

with dilute sulphuric acid as before for a further 21 hours without change. The remainder was sublimed to furnish a crystalline alcohol of m.p. 275°C s.c. The high resolution infra-red spectrum and the GLC behaviour were identical with that of 1-adamantanol (R.I. 1300). A mixed melting point (275° s.c.) was not depressed.

(ii) It was found that the acidic solvolytic action on the anti exomethylene tosylate dissolved in ether, could be effected more rapidly if dilute hydrochloric acid (6N) were used; it was sufficient then to merely wash the ethereal solution twice to effect the same change as above.

Syn-7-exomethylenebicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (100)

A Initial Attempt.

The syn exomethylene alcohol (97, 0.100 g) was treated with toluene-p-sulphonyl chloride (0.138 g, 1.1 M xs) in the corresponding manner (vide supra) and produced a crystalline solid which recrystallised from light petrol as fine needles of m.p. 57-58°C; ν_{max} (mull) 1600, 1380, 1360, 1350, 1195, 1175, 1105, 920, 875, 835, 765 and 685 cm^{-1}. The product was not compatible with that obtained below, and later evidence suggested that isomeration of the double bond had occurred to give syn-7-methylbicyclo(3.3.1)non-6-en-3-yl toluene-p-sulphonate (101).

B Modified procedure.

The syn exomethylene alcohol (97) was treated with toluene-p-sulphonyl chloride and the product isolated as described above for the anti epimer as a colourless solid which recrystallised from pentane as prisms of m.p. 89-89.5°C. Syn-7-exomethylenebicyclo(3.3.1)nonan-3-yl toluene-p-sulphonate (100) ν_{max} (mull) 1650, 1600, 1390, 1360, 1320, 1195, 1185, 1100, 1025, 955, 915, 900, 870, 830, 790 and 680 cm^{-1}; Found, C 66.30 H 7.25. $C_{17}H_{22}SO_3$ requires, C 66.65 H 7.25%. NMR (60 Mc), A_2B_2 quartet @ 2.12-2.72 (4H, aromatic ring)

singlet @ 5.24 (2H, exomethylene) superimposed on an ill-defined multiplet (1H, carbinyl, base width 18 c/s), a sharp singlet @ 7.55 (3H, aromatic methyl), a broad peak @ 7.85 (6H) and a series of 5 peaks @ 8.00-8.80 (6H).

c Effect of mineral acid.

(i) A sample of <u>syn</u> exomethylene tosylate (100, 0.150 g) in ether (30 ml) was shaken with dilute sulphuric acid (6N, 30 ml) and aliquots (10 ml) of the ethereal solution were worked up after 24, 48 and 96 hours as described above. The infra-red spectra of the products were compared with that of starting material: After 24 hours there was little change apart from the broadening of the sharp peak at 900 cm^{-1}. After 48 hours there was absorption at 765 cm^{-1} and strong absorption at 910 cm^{-1}. After 96 hours the product, an oil showed some significant changes; ν_{max} (film) 1740, 1390, 1120, 920s, 810, 765, and 740 cm^{-1} and the bands at 1650, 955 and 790 cm^{-1} were absent. TLC showed that the product was no longer homogeneous; the main component had the same R_f value as the starting material (0.75) but was accompanied by traces of some five other compounds.

(ii) The <u>syn</u> tosylate (100, 0.150 g) in ether (15 ml) was shaken with dilute hydrochloric acid (6N, 15 ml) for 2 hours and the product isolated as an oil which crystallised slowly. Recrystallisation from light petrol produced fine needles of

m.p. 57-59°C; ν_{max} (mull) 1600, 1380, 1360, 1350, 1195, 1175, 1105, 920s, 875, 765 and 685 cm^{-1} (superposable on the product obtained in A above). NMR (60 Mc) in $CDCl_3$, A_2B_2 quartet @ 2.20-2.80 (4H, aromatic ring), doublet centred @ 4.62 (1H, olefinic, J = 6 c/s), an ill defined multiplet @ 5.10 (1H, carbinyl, base width 18 c/s), sharp singlet @ 7.85 (3H, aromatic methyl group), a complex series of small peaks from 7.80-8.40 (10H) and a sharp singlet @ 8.50 (3H, olefinic methyl group). The product was assigned the isomeric structure, syn-7-methylbicyclo(3.3.1)non-6-en-3-yl toluene-p-sulphonate (101).

Anti-7-exomethylenebicyclo(3.3.1)nonan-3-yl Acetate (135)

A sample of the anti exomethylene alcohol (96) was acetylated as described previously and the product isolated as a colourless oil, ν_{max} (film) 3010, 2970, 1725, 1650, 1460, 1380, 1255, 1140, 1035, 990 and 910 cm^{-1}. homogeneous to GLC, R.I. 1375.

Syn-7-exomethylenebicyclo(3.3.1)nonan-3-yl Acetate (136)

A sample of the syn exomethylene alcohol (97) was acetylated as above and the product isolated as a colourless oil, ν_{max} (film) 3010, 2970, 1725, 1650, 1455, 1440, 1380, 1250, 1110, 1100, 1050, 980 and 910 cm^{-1}. homogeneous to GLC, R.I. 1425.

Acetolysis of Anti-7-exomethylenebicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (99)

A solution of anti exomethylene tosylate (0.221 g, 0.72 mM) and fused sodium acetate (0.065 g, 0.79 mM) in anhydrous acetic acid (7.2 ml) was maintained at 50°C for 30 hours. The product was isolated in the usual manner as a colourless oil; ν_{max} (film) 1725, 1250, 1120, 1075 and 1030 cm^{-1}., homogeneous to GLC with R.I. of 1410. The acetate produced was identified as 1-adamantyl acetate by reduction to the alcohol and comparisons with an authentic sample of 1-adamantanol; the high resolution infra-red spectra and GLC behaviour were identical.

There was no evidence of the formation of olefin nor of syn or anti exomethylene acetates (136, 135).

Partial Acetolysis of Anti-7-exomethylenebicyclo(3.3.1)-nonan-3-yl Toluene-p-sulphonate (99)

A solution of anti exomethylene tosylate (0.040 g, 0.13 mM) and fused sodium acetate (0.012 g, 0.14 mM) in anhydrous acetic acid (13 ml) was maintained at 25°C for 8 minutes (approximately 27% reaction, half-life = 17.6 minutes) then the solvolysis was worked up in the manner previously described, using ether-pentane (1:1) to recover the unreacted tosylate and solvolysis product. The infra-red spectrum was superposable on that of starting material with the addition of ν_{max} (film) 1725 and 1250 cm^{-1}.

NMR (100 Mc) in $CDCl_3$: A_2B_2 quartet @ 2.17-2.72 (with enhancement of the last peak due to $CHCl_3$), a nine line multiplet centred @ 4.60 (X part of an A_2B_2X system; J_{AX} = 11c/s, J_{BX} = 6 c/s), a singlet @ 5.35 and a sharp singlet @ 7.58 . The methylene and methine proton resonance was complicated by the presence of solvolysis product (in prominance was a sharp singlet @ 8.08 for the methyl group of 1-adamantyl acetate). The relative integration of these peaks is discussed elsewhere.

The sample was re-run in carbon tetrachloride solution and a centro-symmetric A_2B_2 quartet was observed for the aromatic protons.

Acetolysis of Syn-7-exomethylenebicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (100).

A solution of syn exomethylene tosylate (1.309 g, 4.26mM) and fused sodium acetate (0.385 g, 4.7mM) in anhydrous acetic acid (43 ml) was maintained at 50°C for 60 hours and the products isolated as before, as a colourless oil. The infrared spectrum of the products was essentially identical with that of 1-adamantyl acetate with additional absorption at 3050, 1650, 1035, 910 and 750 cm^{-1}. GLC analysis confirmed the occurrence of 1-adamantyl acetate as the main product (82% by triangulation) accompanied by anti-7-exomethylene-bicyclo(3.3.1)nonan-3-yl acetate (13S, 3%, R.I. 1375) and an olefin (15%, R.I. 1100). There was no evidence of syn

exomethylene acetate (136) in the products.

The major portion of the reaction products was chromatographed on grade III neutral alumina and elution with pentane afforded both the olefin (r_f 1.0) and the mixture of acetates (r_f 0.8) however the first fraction (30 mg) was essentially pure olefin; ν_{max} (film) 3050, 2920, 1650, 1470, 1440, 910s and 750 cm^{-1}. with slight acetate absorption at 1725, 1250 amd 1050 cm^{-1}.

NMR (60 Mc) in pentane: an asymmetric complex signal @ 4.45, 4.50, 4.58 and 4.68 (2H, a degenerate AB system*) and two singlets of equal intensity @ 5.25 and 5.35 (1H each, asymmetric exomethylene group) broad peaks @ 7.60 and 7.75 merging into solvent resonance @ 8.40-9.30 . The olefin was assigned the structure 7-exomethylenebicyclo-(3.3.1)non-2-ene (137).

*A similar signal is observed in the NMR spectrum of bicyclo(3,3,1)non-2-ene (138). (Section I).

Anti-7-spirocyclopropylbicyclo(3.3.1)nonan-3-ol (112)

Anti-7-exomethylenebicyclo(3,3,1)nonan-3-ol (0.25 g, 1.65 mM) and methylene iodide (0.88 g, 3.3.mM) dissolved in ether (5 ml) were slowly added to a stirred solution of zinc-copper couple (1.76 g, prepared according to the method of Shank [133]), in anhydrous ether (45 ml). The reaction was heated under reflux for 48 hours then worked up following the method of Winstein [99] to produce a yellow oil (0.50 g). TLC indicated the presence of methylene iodide (r_f 0.8) and the main product (r_f 0.3) and also traces of 3 other compounds (r_f 0.0, 0.7 and 0.9). GLC analysis indicated that the reaction mixture contained equal amounts of anti-7-spirocyclopropylbicyclo(3,3,1)nonan-3-ol (112, R.I. 1385) and starting material, anti exomethylene alcohol (96, R.I. 1325).

The crude product was adsorbed on grade IV basic alumina; elution with 20% ether-pentane gave mixtures of the cyclopropyl and exomethylene alcohols (3 fractions) homogeneous to TLC but readily monitored by GLC analysis on Apiezon L at 150°C. The fractions enriched in product were combined (125 mg) and re-chromatographed on commercial silver nitrate/silica (15 g). Elution with 40% ether-pentane effected a separation of product (38 mg) homogeneous to GLC. Fractions containing both cyclopropyl and exomethylene alcohols (61 mgs) were set aside.

The chromatographed product was sublimed to furnish anti-7-spirocyclopropylbicyclo(3,3,1)nonan-3-ol (112) as stout prisms of m.p. 90-90.5°C; ν_{max} (CCl_4, high resolution) 3627a, 3063, 2986, 2956, 2913, 2839a, 1455, 1439, 1416, 1363, 1314, 1265, 1176, 1036, 1012, 988, 961, 938 and 919 cm^{-1}. Found: C 79.05, H 10.60. $C_{11}H_{18}O$ requires; C 79.45, H 10.90%. Mass spectral parent ion, 166. NMR (100 Mc) in $CDCl_3$, internal reference; benzene. A nine line multiplet @ 5.20 (1H, X part of an A_2B_2X system; J_{AX} = 11.0 c/s, J_{BX} = 6.0 c/s), two overlapping broad peaks @ 7.90 and 7.98 (6H), a broad singlet @ 8.50 (4H) with a sharp singlet superimposed @ 8.63 (1H, hydroxyl), a doublet centred @ 9.06 (2H, J = 12 c/s) and a centrosymmetric A_2B_2 quartet @ 9.55, 9.61, 9.68 and 9.74 (4H, cyclopropyl).

Anti-7-spirocyclopropylbicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (115).

Treatment of anti-7-spirocyclopropylbicyclo(3,3,1)-nonan-3-ol (112) with toluene-p-sulphonyl chloride in the manner described for the exomethylene series provided the corresponding tosylate (115) as colourless crystals which recrystallised from pentane to give plates (0.010 g) of m.p. 68.5-70.5°C; ν_{max} (mull) 1355, 1345, 1180, 935, 870, 785 and 680 cm^{-1}.

Acetolysis of
Anti-7-spirocyclopropylbicyclo(3.3.1)nonan-3-yl
Toluene-p-sulphonate (115).

Two solutions of anti-7-spirocyclopropylbicyclo(3,3,1)-nonan-3-yl tosylate (approx. 3 mg) in buffered anhydrous acetic acid (3 mls, 4.38 x 10^{-3} M in sodium acetate) were maintained at 25° and 50°C respectively for 10 half-lives in the course of two kinetic runs (appendix A). The reaction product was isolated in the usual manner as a colourless oil (4.0 mg) homogeneous to GLC with retention index of 1555. The product was identified as 3-homoadamantyl acetate by reduction to the alcohol (R.I. 1435) and comparison with an authentic sample of 3-homoadamantanol (R.I. 1435), kindly supplied by Professor P. von R. Schleyer. The mass spectrum (GCMS) of the alcohol derived from solvolysis was identical with that of 3-homoadamantanol.

Simmons-Smith [117] Reaction on Syn-7-exomethylenebicyclo(3.3.1)nonan-3-ol (97).

The syn alcohol 95, (0.100 g, 0.66 mM) was treated with methylene iodide (0.354 g, 1.32 mM) and zinc-copper couple (0.70 g) in anhydrous ether. The reaction was heated under reflux for 2 hours and the product isolated as before. TLC indicated that the fragrant yellow oil contained methylene iodide and a product of similar polarity; there was no trace of starting alcohol. The reaction mixture was chromatographed but failed to give product completely free from methylene iodide. The product had no hydroxyl absorption in the infra-red spectrum. GLC analysis resolved the product (R.I. 1195) and the mass spectrum (GCMS) showed a parent ion at 152 (98% of the base peak). NMR (60 Mc): a sharp singlet @ 6.10 (CH_2I_2) superimposed on an ill-defined multiplet (1H?), three broad peaks @ 7.96 (2H), 8.22 (4H) and 8.40 (6H), and a sharp singlet @ 9.03 (3H, methyl group). The product was tentatively assigned the structure 1-methyl-2-oxoadamantane (114).

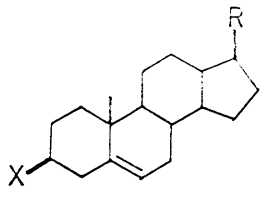
A small quantity of pure material was obtained as a colourless oil by sacrificial sublimation; ν_{max} (film) 2950, 2810, 1450, 1390, 1340, 1205, 1150, 1105, 1065, 1030, 900, 830 and 755 cm^{-1}. The product was identical with material prepared below.

Acid-catalysed Isomeration of
Anti-7-exomethylenebicyclo(3.3.1)nonan-3-ol (96).

The isomeration of the anti exomethylene alcohol in 75% sulphuric acid to give 7-exo-methylbicyclo(3,3,1)nonan-3-one (139) has been described in Section I.

Acid catalysed Isomeration of
Syn-7-exomethylenebicyclo(3.3.1)nonan-3-ol (97).

Treatment of the syn exomethylene alcohol in 75% sulphuric acid as described previously produced a colourless oil, homogeneous to TLC and GLC (R.I. 1195); ν_{max} (CCl_4, high resolution) 2920, 2845, 2660, 1440, 1375, 1325, 1205, 1135, 1095, 1045, 1010, 960, 930, 875, 805 and 730 cm^{-1}. NMR (100 Mc): a multiplet centred @ 6.08 (1H, base width 12 c/s), three broad peaks @ 7.87, 8.17 and 8.40 and a sharp methyl singlet @ 8.97 . The product was assigned the structure 1-methyl-2-oxoadamantane (114).



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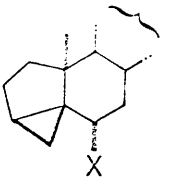

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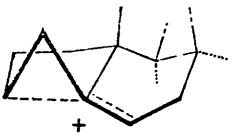

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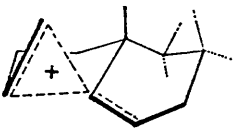

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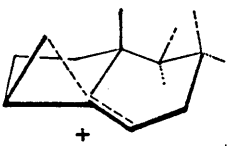

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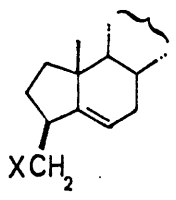

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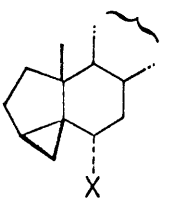

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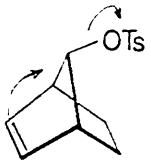

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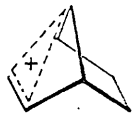

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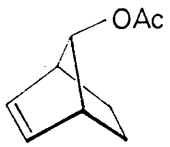

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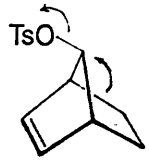

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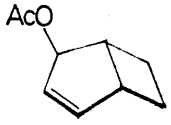

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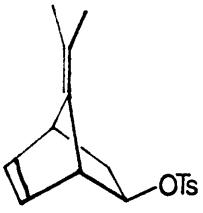

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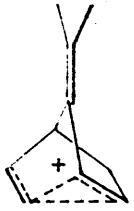

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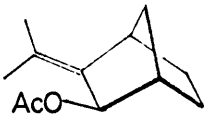

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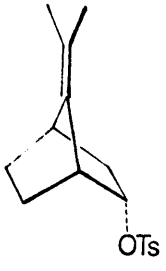

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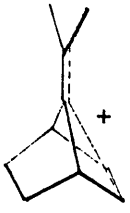

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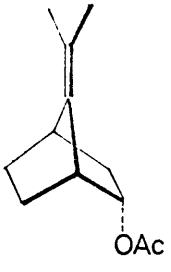

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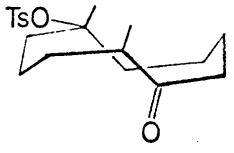

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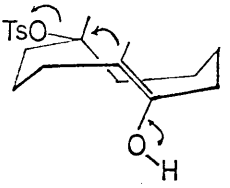

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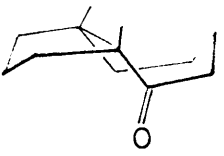

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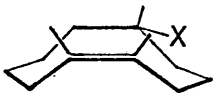

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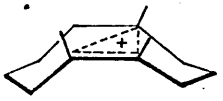

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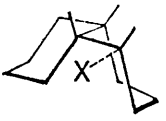

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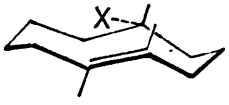

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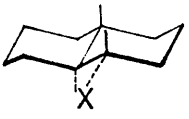

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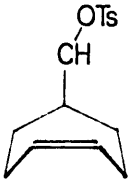

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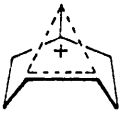

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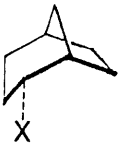

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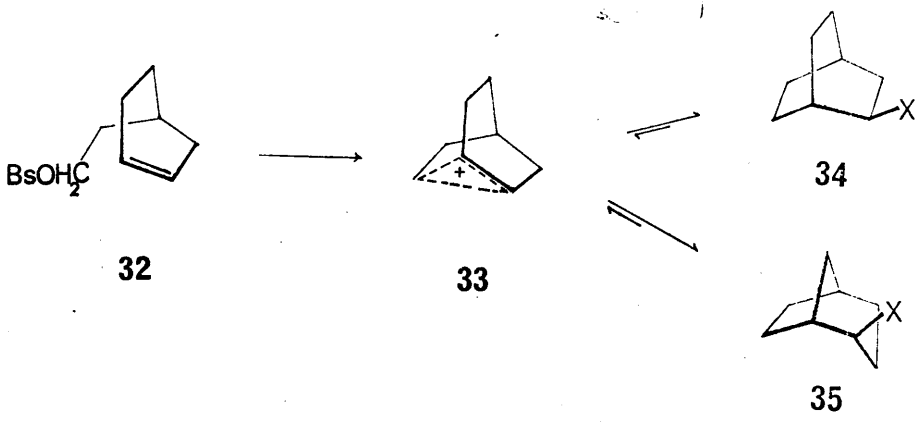

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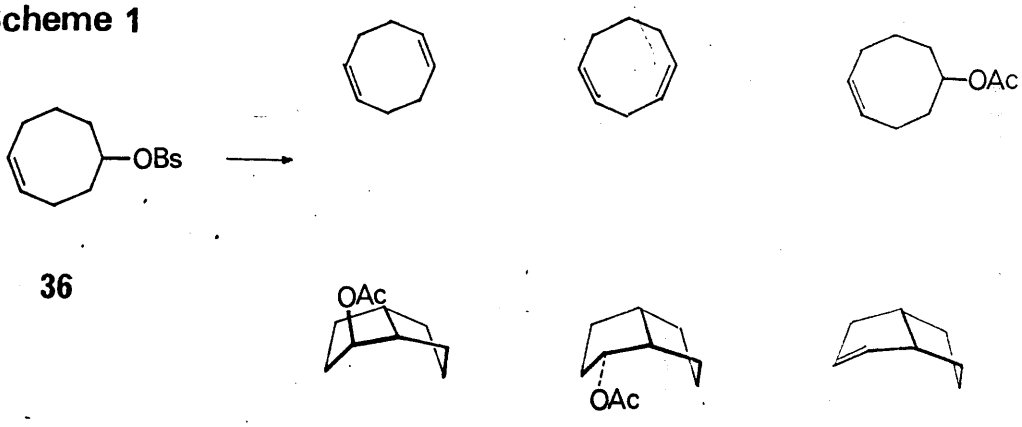
Scheme 1



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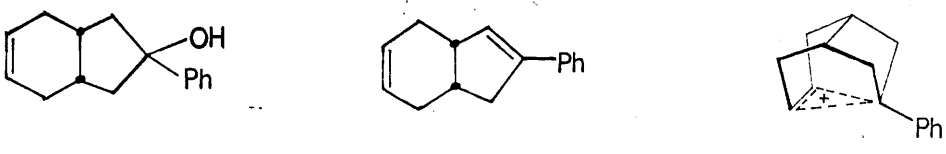

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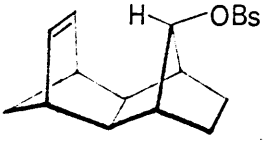

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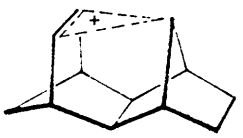

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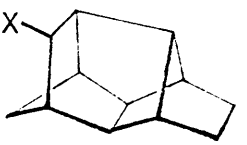

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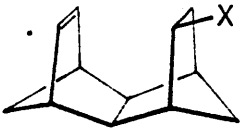

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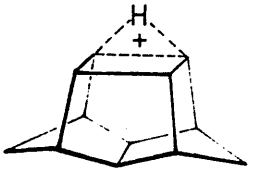

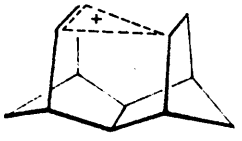

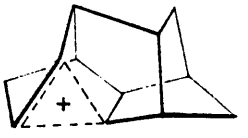

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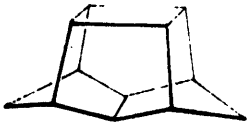

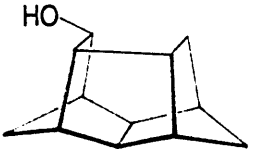

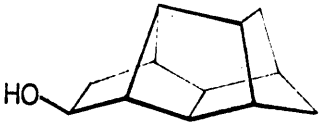

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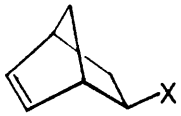

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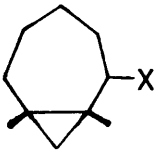

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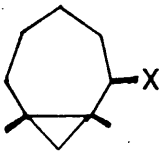

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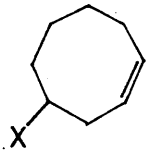

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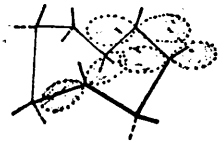

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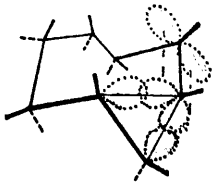

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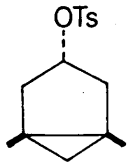

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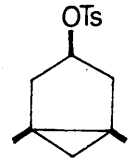

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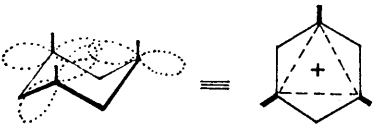

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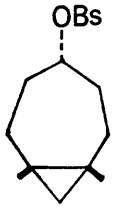

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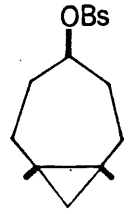

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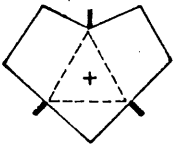

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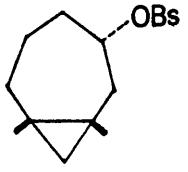

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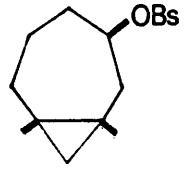

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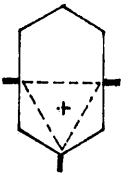

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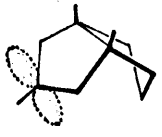

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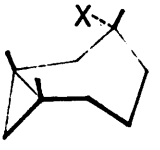

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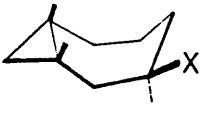

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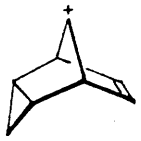

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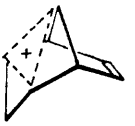

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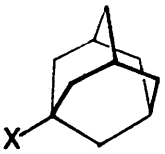

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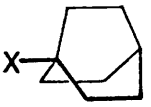

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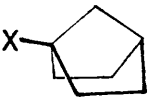

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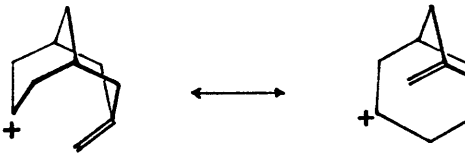

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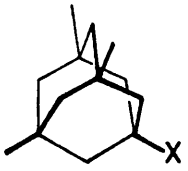

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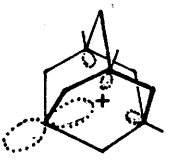

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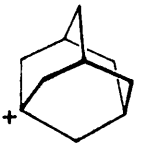

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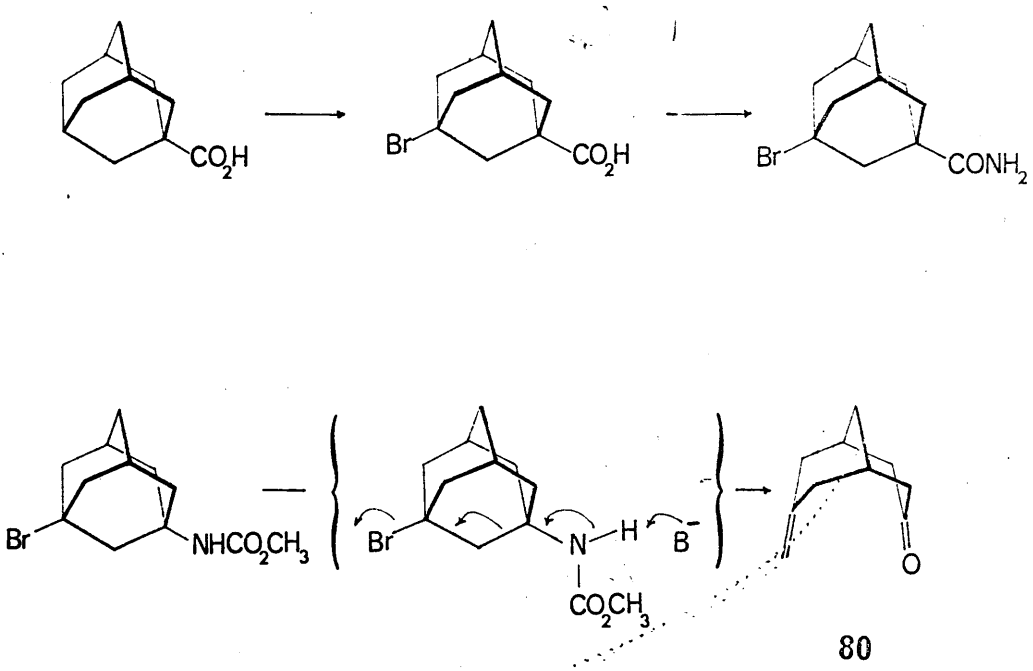
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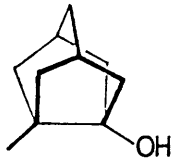

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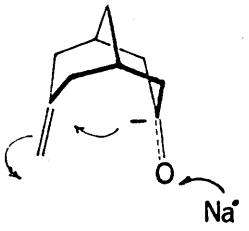

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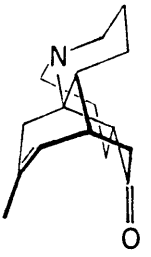

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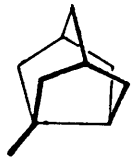

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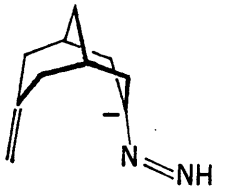

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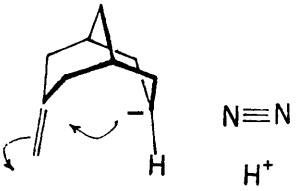

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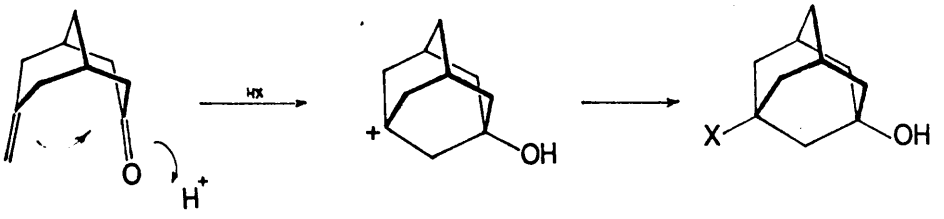

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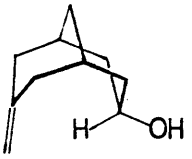

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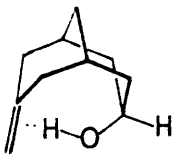

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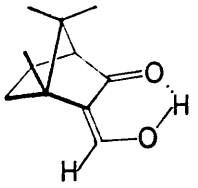

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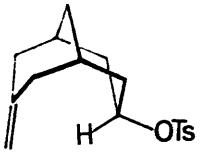

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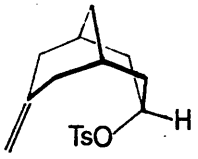

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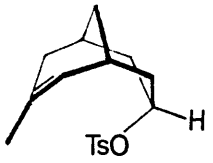

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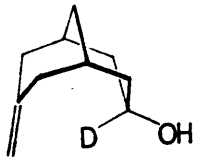

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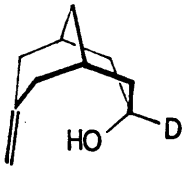

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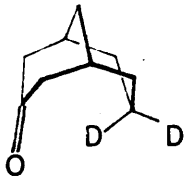

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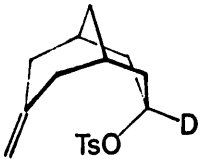

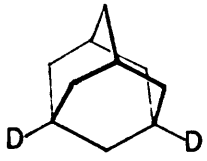

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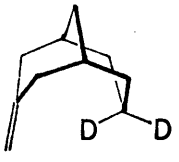

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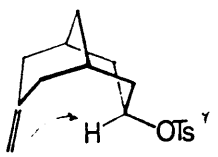

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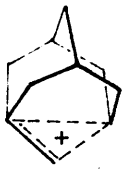

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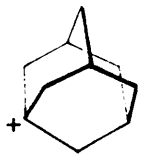

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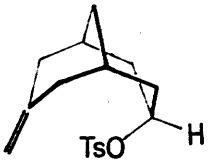

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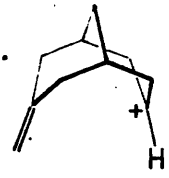

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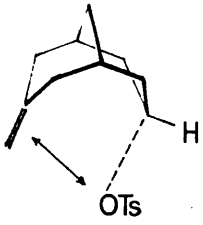

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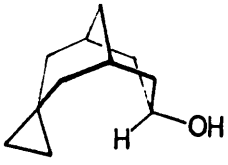

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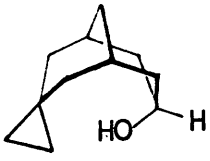

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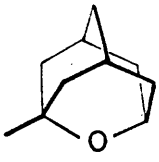

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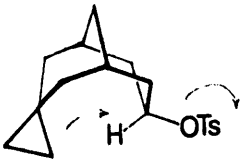

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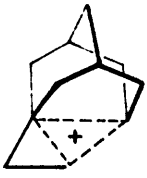

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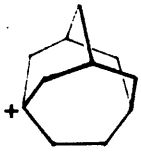

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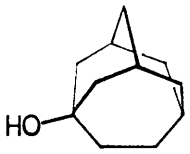

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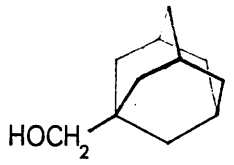

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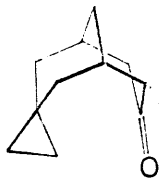

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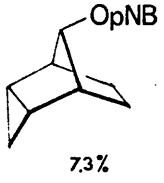

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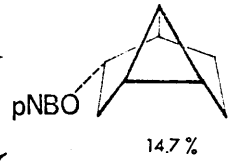

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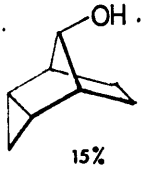

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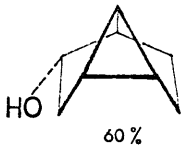

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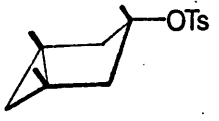
Scheme 3



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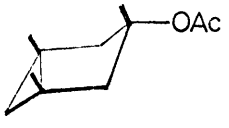

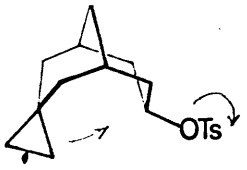

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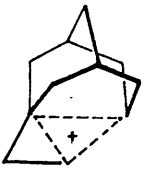

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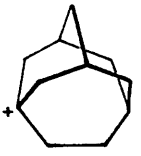

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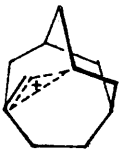

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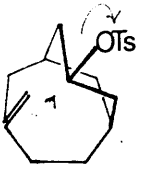

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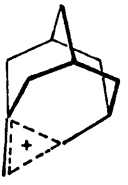

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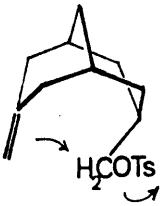

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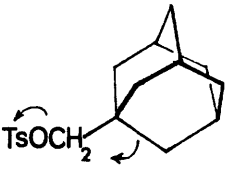

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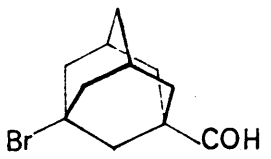

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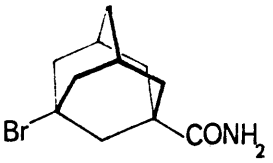

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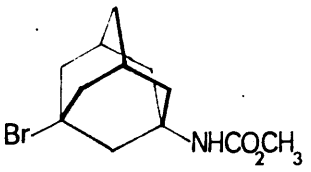

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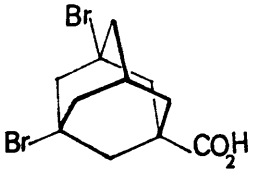

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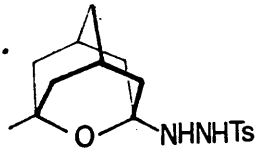

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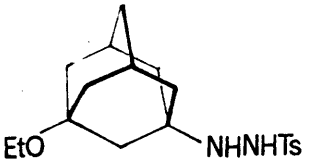

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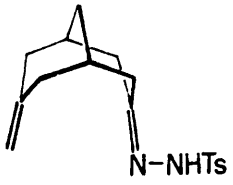

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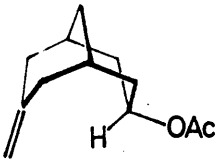

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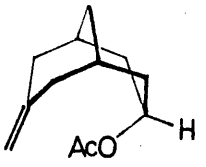

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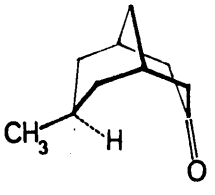

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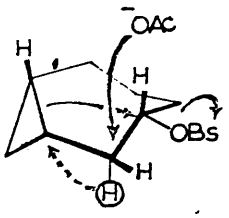
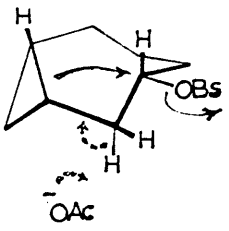
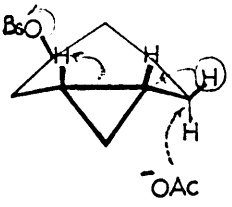
FIG. 10

64  D.

64  C.

65  E.

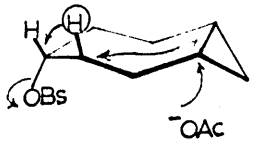
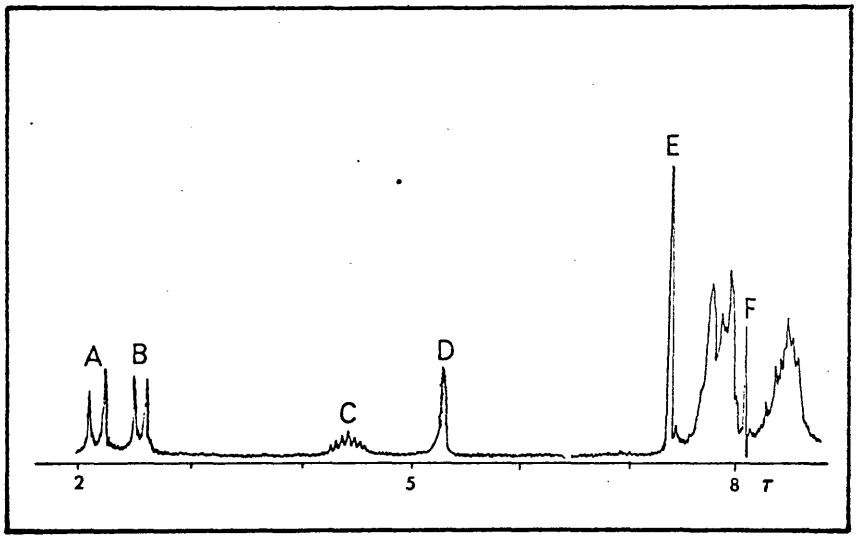
61  J.

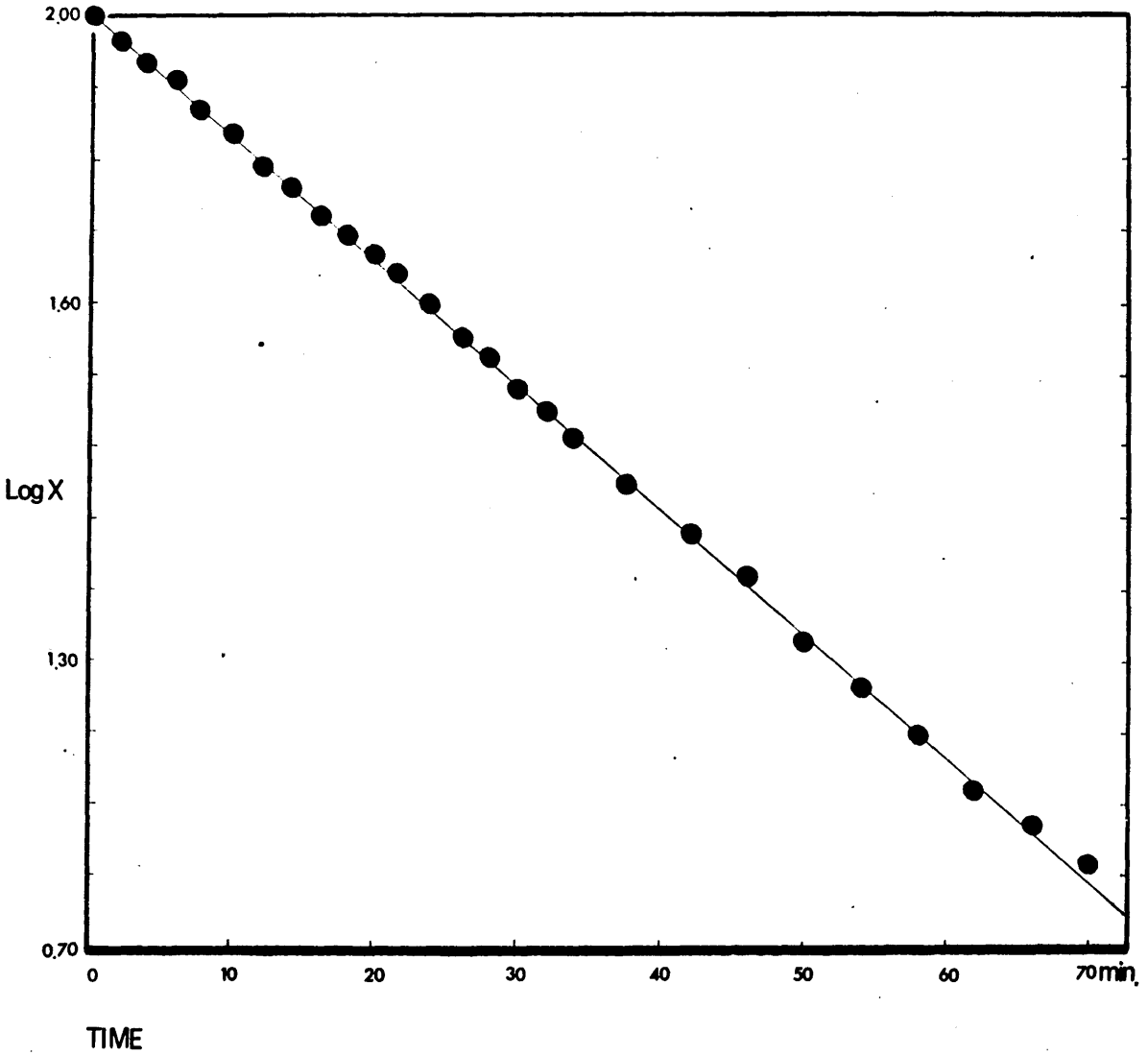
FIG. 11

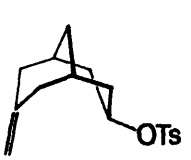
100 Mc. NMR Spectrum of the compounds isolated from the partial Acetolysis of Anti-7-exomethylenebicyclo(3,3,1)nonan-3-yl Toluene-p-sulphonate.



Integration Data.

Peak	INTEGRATION.		
	(i)	(ii)	(iii)
A	23	9	24
B	30	11.5	31
C	11	4	11
D	22	9	22
E	34	13	35
(A+E)/5	11.4	4.40	11.8
(C+D)/3	11.0	4.33	11.0
Tosylate 99,	96.5%	98.5%	93.0%





at 25°C

APPENDIX A

RATE MEASUREMENTS.

Acetolysis of Anti-7-exomethylenebicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (99)

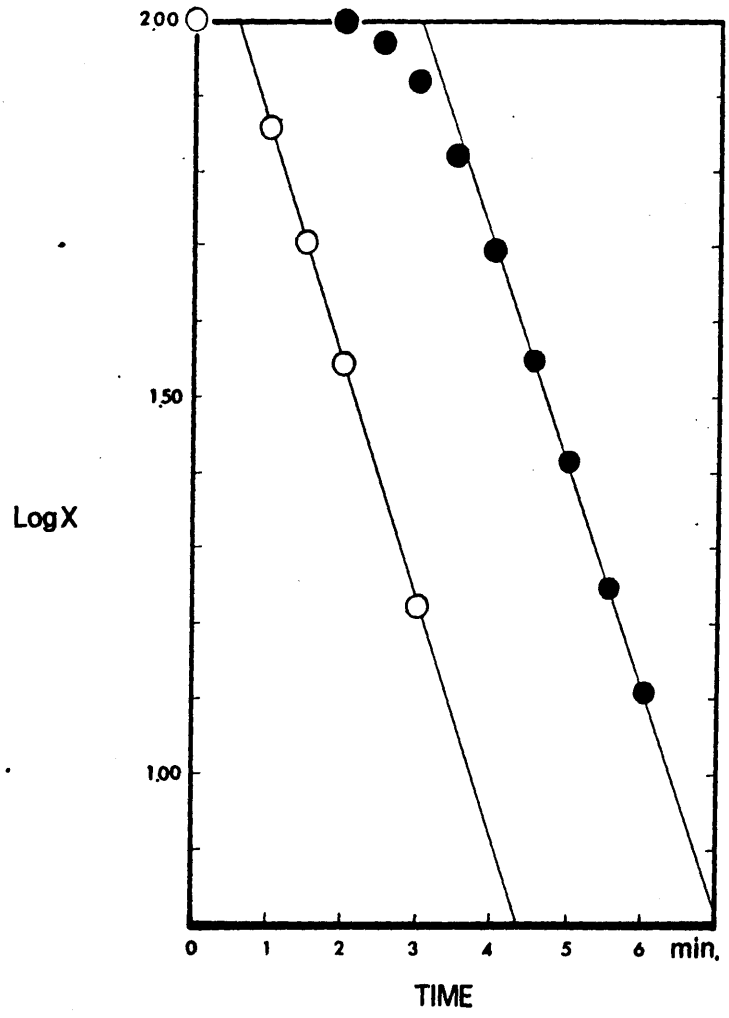
ROTs : 3.52×10^{-3}M Temperature : 25.0°C (±0.1)

NaOAc : 4.70×10^{-3}M

Time (min.)	O.D.	X.	Log X.
0	1.855	100.0	2.000
2	1.800	91.0	1.9595
4	1.770	85.9	1.934
6	1.735	80.3	1.9045
8	1.690	72.7	1.862
10	1.660	67.8	1.8315
12	1.620	61.2	1.787
14	1.595	57.0	1.756
16	1.570	52.9	1.724
18	1.545	48.75	1.688
20	1.530	46.3	1.666
22	1.505	42.2	1.6255
24	1.485	38.9	1.590
26	1.465	35.5	1.551
28	1.450	33.05	1.519
30	1.430	29.75	1.4735
32	1.420	28.1	1.449
34	1.405	25.6	1.4085
38	1.385	22.3	1.349
42	1.365	19.0	1.279
46	1.350	16.5	1.218
50	1.330	13.2	1.122
54	1.320	11.58	1.0635
58	1.310	9.92	0.997
62	1.300	8.26	0.9175
66	1.295	7.44	0.872
70	1.290	6.51	0.820
180	1.250	0.0	-

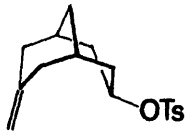
From graph; $t_{\frac{1}{2}} = 17.6$ mins.

$k = 6.56 \times 10^{-4}$ sec^{-1}.



○ RUN A
● RUN B

at 50°C



Acetolysis of Anti-7-exomethylenebicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (99).

ROTs : 3.78×10^{-3}M Temperature : 50.0°C (±0.15)

NaOAc : 4.4×10^{-3}M

Time (min.)	O.D.	X.	Log X.
0	1.443	100.0	2.000
1	1.410	73.2	1.865
2	1.363	35.0	1.540
3	1.340	16.25	1.211
4	1.330	8.10	0.909
6	1.325	4.06	0.609
20	1.320	0.0	-

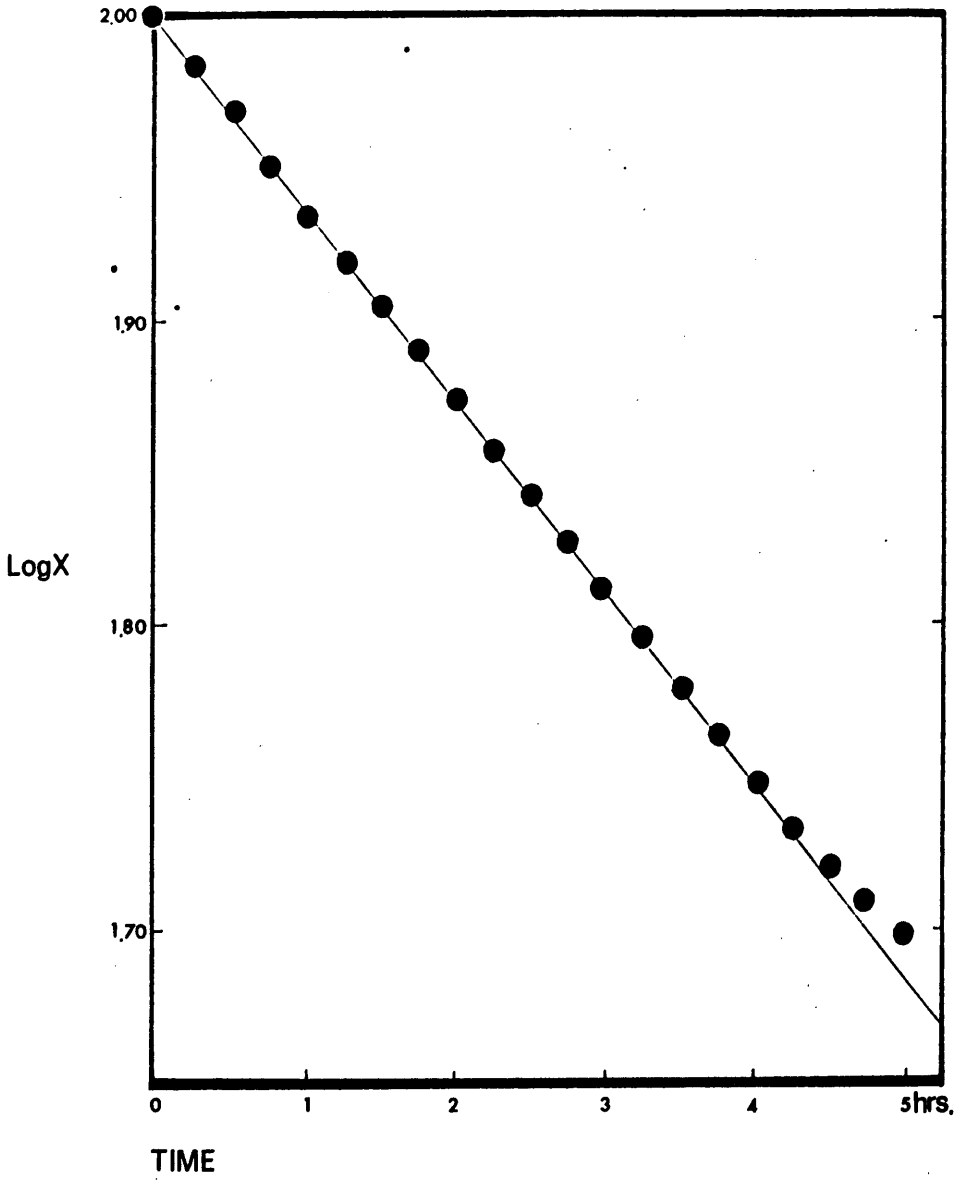
ROTs ; 3.92×10^{-3}M

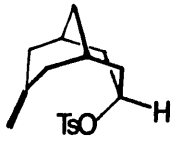
NaOAc : 4.90×10^{-3}M

0.0	1.980	100.0	2.000
0.5	1.935	92.8	1.968
1.0	1.880	83.05	1.920
1.5	1.780	66.2	1.821
2.0	1.680	49.2	1.692
2.5	1.600	35.6	1.552
3.0	1.542	25.6	1.408
3.5	1.495	17.7	1.248
4.0	1.465	12.7	1.104
20.0	1.390	0.0	-

From graphs: $t_{\frac{1}{2}} = 1.00$ min.

$k = 1.15 \times 10^{-2}$ sec^{-1}.





at 25°C

Acetolysis of Syn-7-exomethylenebicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (100).

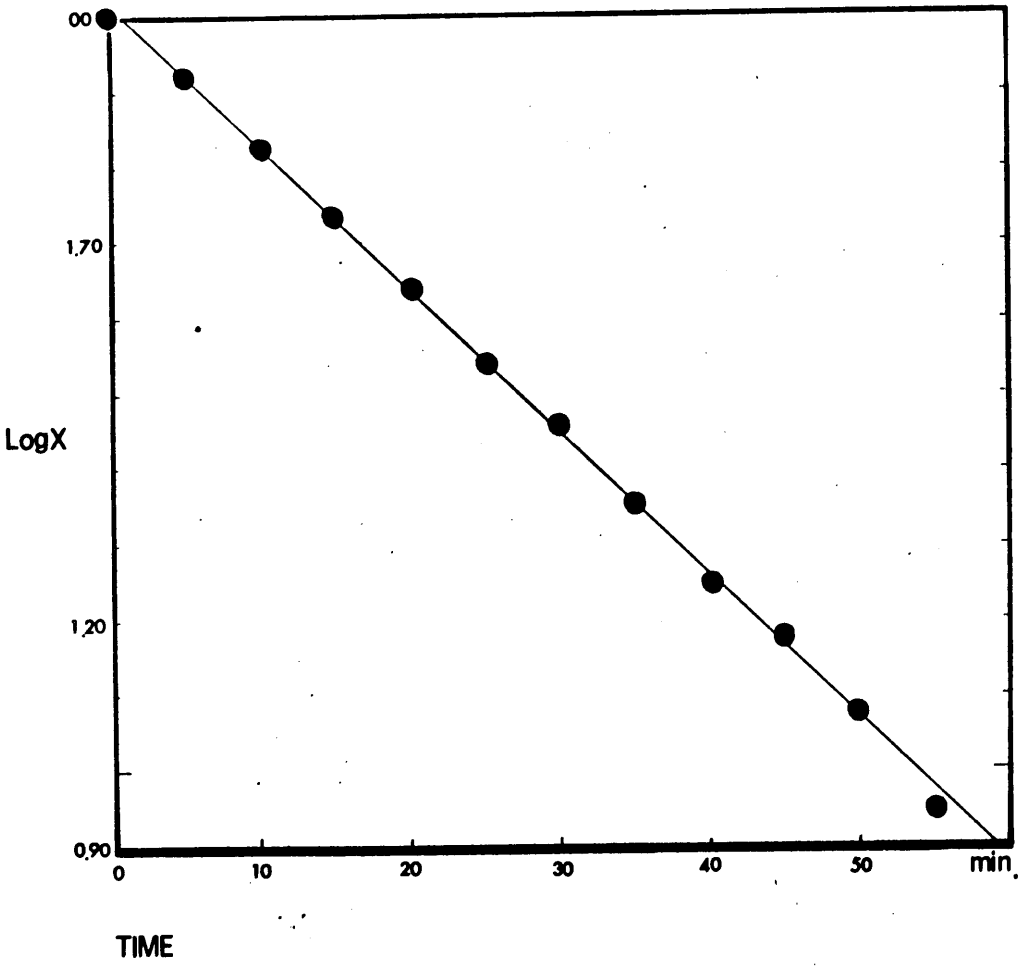
ROTs : 2.195×10^{-3}M Temperature : 25.0°C (± 0.1)

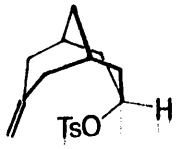
NaOAc : 3.38×10^{-3}M Scan Interval : 15.0 min.

Scan.	O.D.	X.	Log X.
0	1.320	100.0	2.000
1	1.300	96.2	1.9835
2	1.282	92.6	1.9675
3	1.264	88.8	1.949
4	1.246	85.6	1.933
5	1.230	82.75	1.918
6	1.215	79.8	1.9025
7	1.200	76.9	1.886
8	1.186	74.3	1.871
9	1.173	71.8	1.856
10	1.160	69.4	1.841
11	1.148	67.0	1.826
12	1.136	64.6	1.8105
13	1.124	62.3	1.7945
14	1.112	60.0	1.7785
15	1.100	57.7	1.762
16	1.090	55.8	1.747
17	1.080	53.9	1.732
18	1.073	52.5	1.720
19	1.066	51.2	1.709
20	1.060	50.0	1.699
	0.800	0.0	-

From graph: $t_{\frac{1}{2}} = 4.75$ hours

$k = 4.05 \times 10^{-5}$ sec^{-1}.





at 50°C

Acetolysis of Syn-7-exomethylenebicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (100).

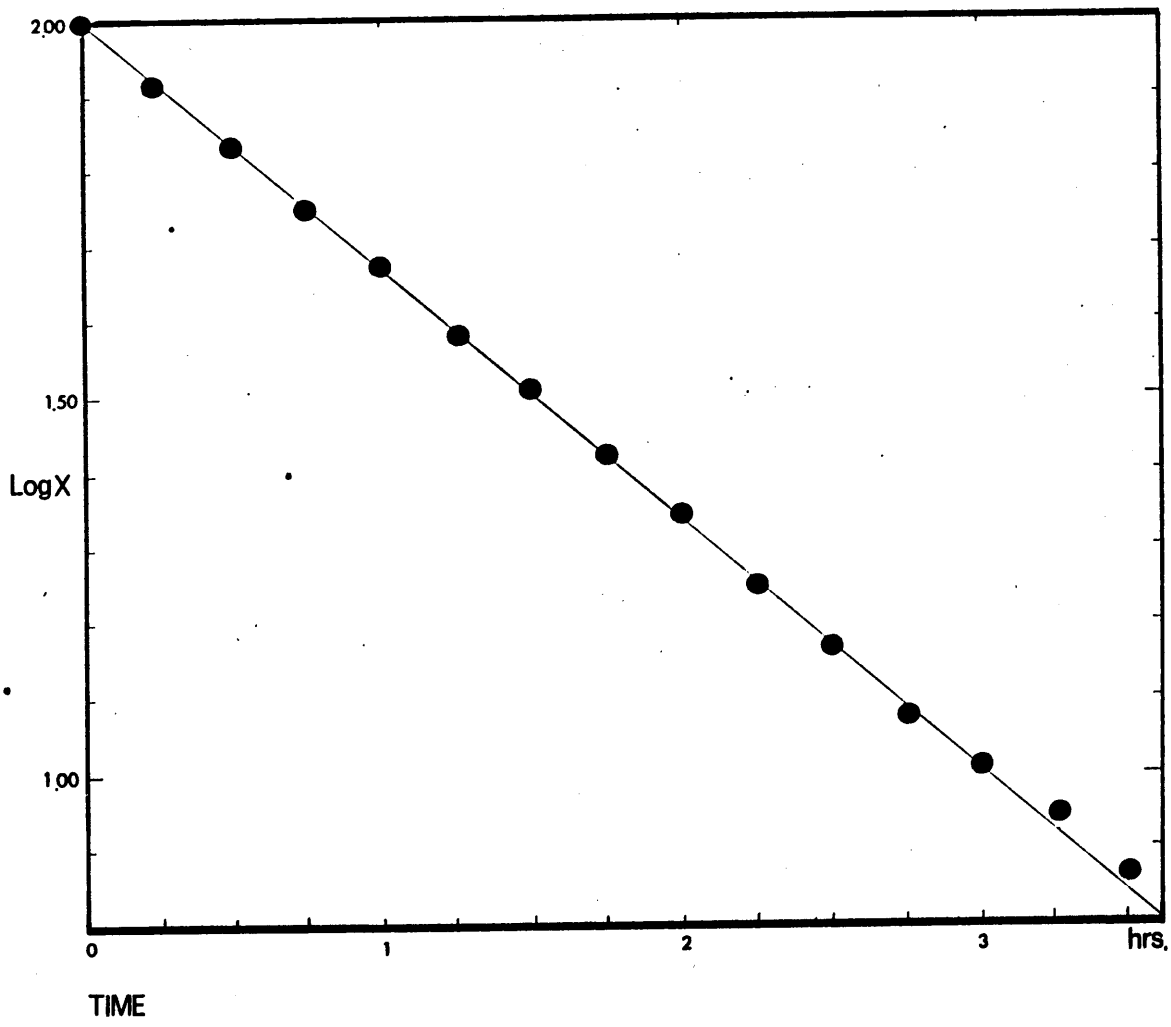
ROTs : 3.11×10^{-3}M. Temperature: 50.0°C (±0.15)

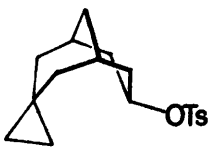
NaOAc : 3.68×10^{-3}M.

Time (min)	O.D.	X.	LogX.
0	1.775	100.0	2.000
5	1.670	83.15	1.920
10	1.565	66.4	1.822
15	1.490	54.4	1.735
20	1.420	43.2	1.636
25	1.365	34.4	1.537
30	1.328	28.5	1.455
35	1.290	22.4	1.351
40	1.260	17.6	1.246
45	1.240	14.4	1.158
50	1.224	11.75	1.070
55	1.204	8.8	0.945
	1.150	0.0	-

From graph: $t_{\frac{1}{2}} = 15.50$ min.

$k = 7.45 \times 10^{-4}$ sec^{-1}.





at 25°C

Acetolysis of Anti-7-spirocyclopropylbicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (115)

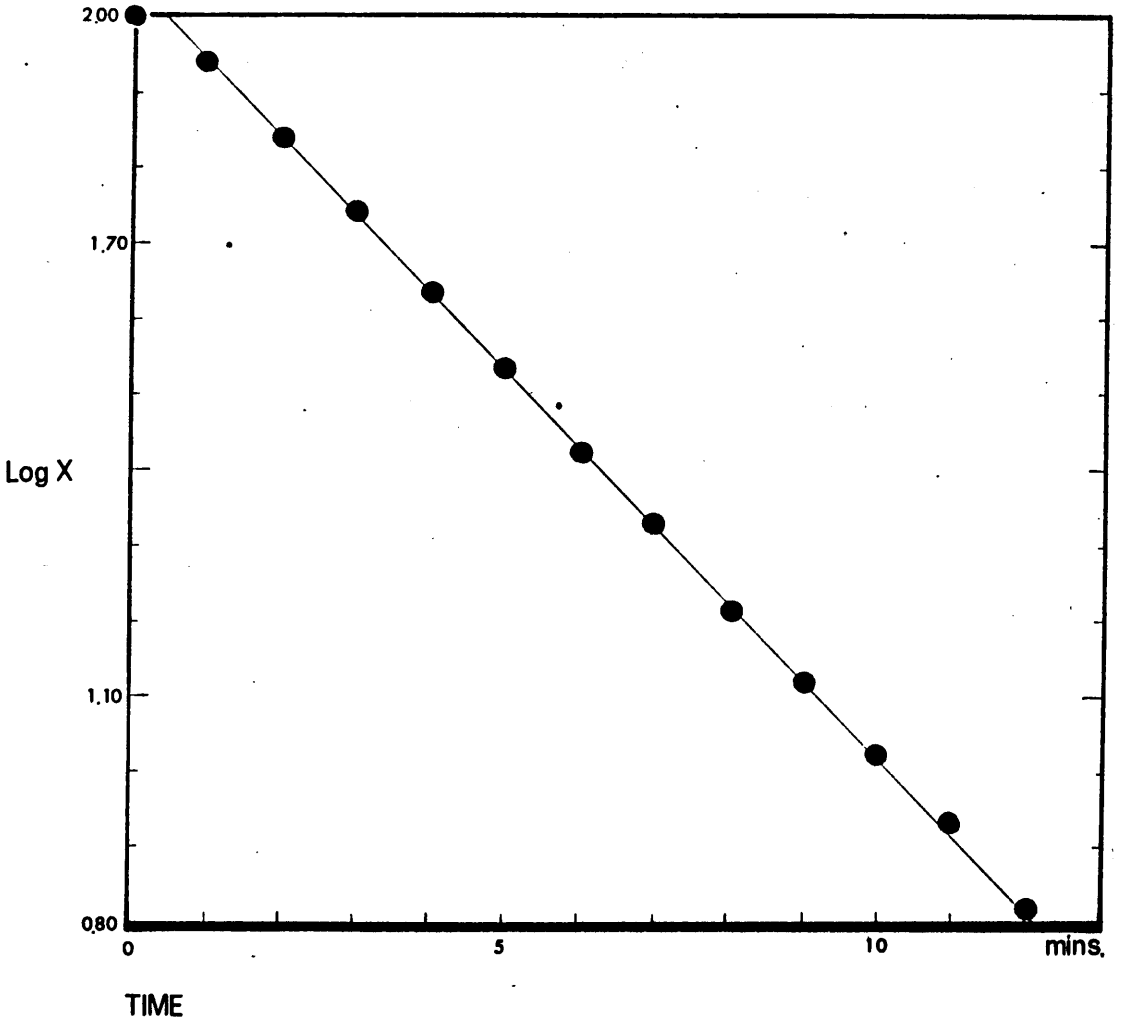
ROTs : 3.0×10^{-3}M. Temperature : 25.0°C (± 0.1)

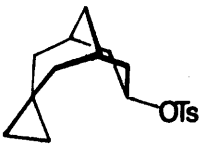
NaOAc : 4.38×10^{-3}M.

Time (min.)	O.D.	X.	Log X.
0	1.700	100.0	2.000
15	1.640	82.5	1.916
30	1.590	67.6	1.8305
45	1.550	55.9	1.7475
60	1.520	47.1	1.673
75	1.490	38.2	1.582
90	1.470	32.4	1.510
105	1.450	26.4	1.422
120	1.435	22.0	1.343
135	1.420	17.65	1.246
150	1.410	14.7	1.168
165	1.400	11.75	1.071
180	1.395	10.3	1.012
195	1.390	8.3	0.946
210	1.395	7.35	0.867
600	1.360	0.0	-

From Graph; $t_{\frac{1}{2}} = 54.0$ min.

$k = 2.14 \times 10^{-4}$ seo^{-1}.





at 50°C

Acetolysis of Anti-7-spirocyclopropylbicyclo(3.3.1)nonan-3-yl Toluene-p-sulphonate (115).

ROTs : 3.0×10^{-3}M Temperature : 50.0°C (± 0.15)

NaOAc : 4.38×10^{-3}M

Time (min.)	O.D.	X.	Log X.
0	1.760	100.0	2.000
1	1.710	86.8	1.938
2	1.640	69.4	1.8355
3	1.590	55.3	1.743
4	1.545	43.4	1.6375
5	1.510	34.2	1.5345
6	1.480	26.3	1.420
7	1.460	21.05	1.323
8	1.442	16.3	1.212
9	1.430	13.15	1.119
10	1.420	10.5	1.022
11	1.413	8.68	0.939
12	1.405	6.59	0.819
60	1.380	0.0	-

From graph: $t_{\frac{1}{2}} = 2.90$ min.

$k = 3.98 \times 10^{-3}$ sec^{-1}.

APPENDIX B

GLC DATA

COMPOUND	COLUMN	TEMP.	FLOW RATE	RET. TIME (OR INDEX)
88	20% TCEP.	50°C	55ml/min.	3.3 min.
73(X=H)	"	"	"	9.1
137	20% $AgNO_3$.	"	35	8.0
85	5% Carbowax.	125°C	40	5.65
114	"	"	"	9.4
97	"	"	"	11.3
73(X=H)	"	"	"	12.8
80	"	"	"	15.3
96	"	"	"	21.2
118	"	"	"	25.2
113	"	"	"	26.2
80	10% 20M PEG/	"	"	2.4
85	Carbowax.	"	"	3.1
97	"	"	"	6.1
73(X=OH)	"	"	"	6.4
96	"	"	"	9.4
85	10% PEGA	150°C	"	1.8
73(X=OH)	"	"	"	3.35
97	"	"	"	3.5
96	"	"	"	4.75
80	"	"	"	5.0
92(X=OiPr)	"	"	"	13.4
92(X=OH)	"	"	"	38.0
137	10% ApL.	125°C	50	1100
114	"	"	"	1190
85	"	"	"	1195
73(X=OH)	"	"	"	1300
80	"	"	"	1325
96	"	"	"	1325
97	"	"	"	1325
112	"	"	"	1385
119	"	"	"	1420
118	"	"	"	1435
135	"	"	"	1375
73(X=OAc)	"	"	"	1410
136	"	"	"	1425
118(OAc)	"	"	"	1555

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